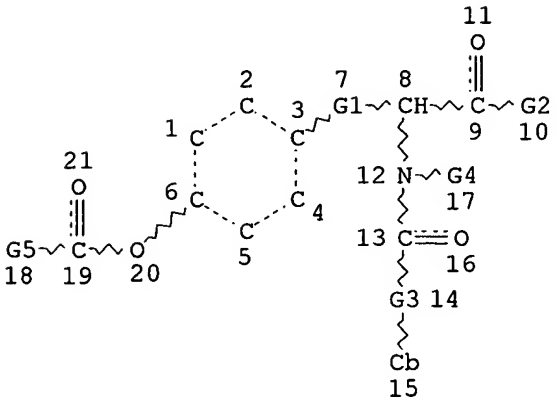
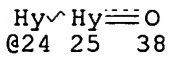
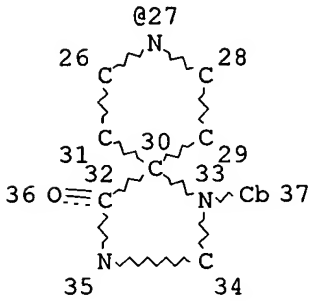
(FILE 'REGISTRY' ENTERED AT 10:52:39 ON 26 APR 2005)

L11 STR



Hy @22 Hy @23





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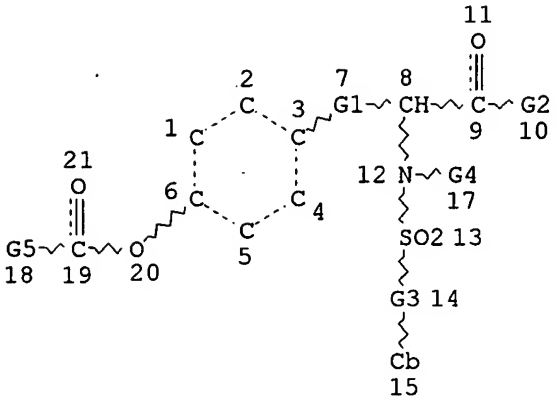
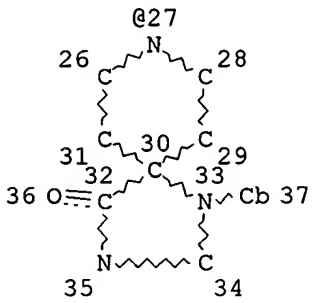
REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/23/24/27
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
GGCAT IS MCY AT 22
GGCAT IS PCY AT 23
GGCAT IS MCY AT 24
GGCAT IS PCY AT 25
GGCAT IS UNS AT 37
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E4 C E2 N AT 22
ECOUNT IS E9 C E1 N AT 23
ECOUNT IS E5 C E1 N AT 24
ECOUNT IS E2 N AT 25

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE
L12 STR



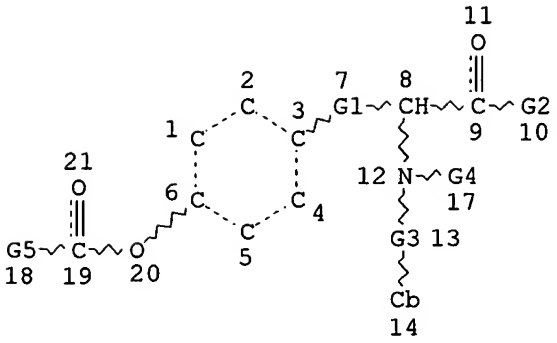
Hy @22 Hy @23 Hy Hy O
@24 25 38



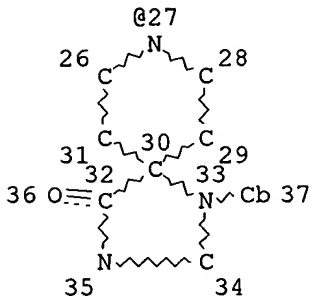
REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/23/24/27
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
GGCAT IS MCY AT 22
GGCAT IS PCY AT 23
GGCAT IS MCY AT 24
GGCAT IS PCY AT 25
GGCAT IS UNS AT 37
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E4 C E2 N AT 22
ECOUNT IS E9 C E1 N AT 23
ECOUNT IS E5 C E1 N AT 24
ECOUNT IS E2 N AT 25

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 37

STEREO ATTRIBUTES: NONE
L13 STR



Hy @22 Hy @23 Hy Hy O
@24 25 38



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REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/23/24/27
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GGCAT IS PCY AT 25
GGCAT IS UNS AT 37
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E4 C E2 N AT 22
ECOUNT IS E9 C E1 N AT 23
ECOUNT IS E5 C E1 N AT 24
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE
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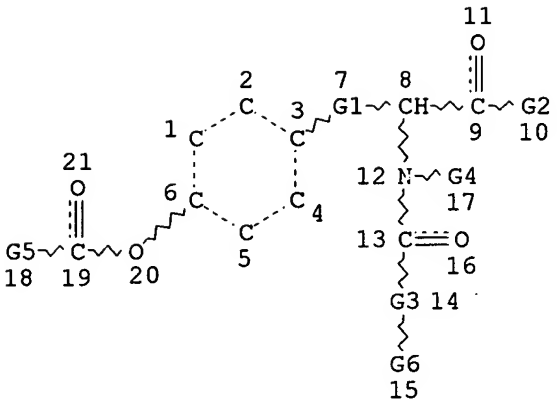
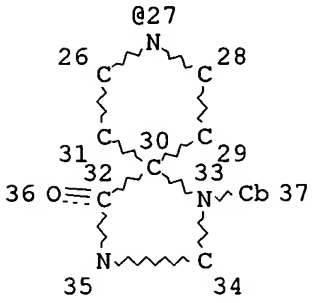


Hy @22 Hy @23 Hy Hy O
@24 25 38



Ak CN
@39 40

REP G1=(1-2) CH2
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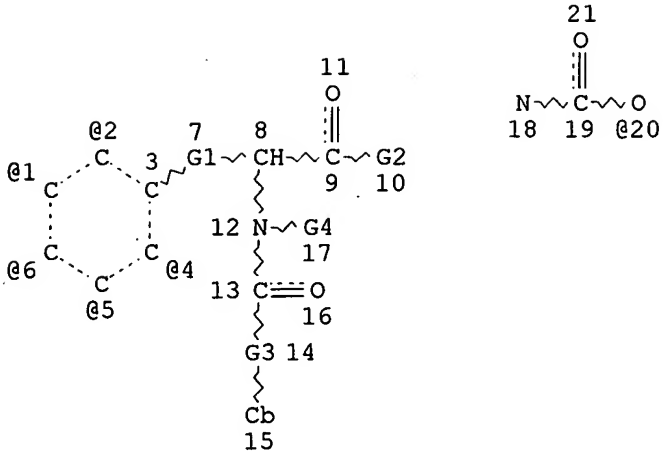
REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/23/24/27
VAR G6=39/CY
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY AT 22
GGCAT IS PCY AT 23
GGCAT IS MCY AT 24
GGCAT IS PCY AT 25
GGCAT IS UNS AT 37
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS E4 C E2 N AT 22
ECOUNT IS E9 C E1 N AT 23
ECOUNT IS E5 C E1 N AT 24
ECOUNT IS E2 N AT 25

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 40

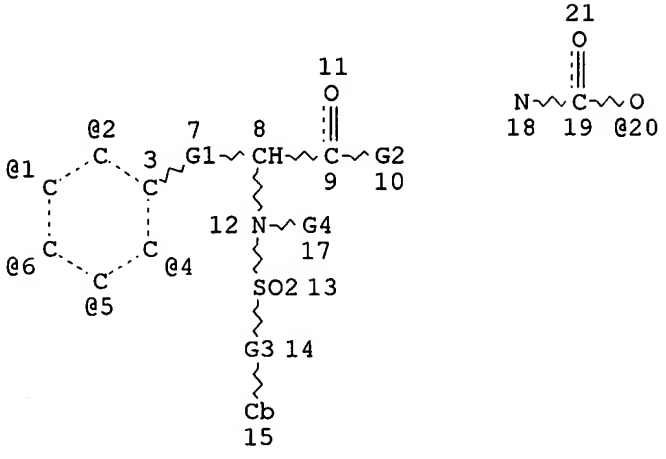
STEREO ATTRIBUTES: NONE
L15 STR



REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
L16 STR

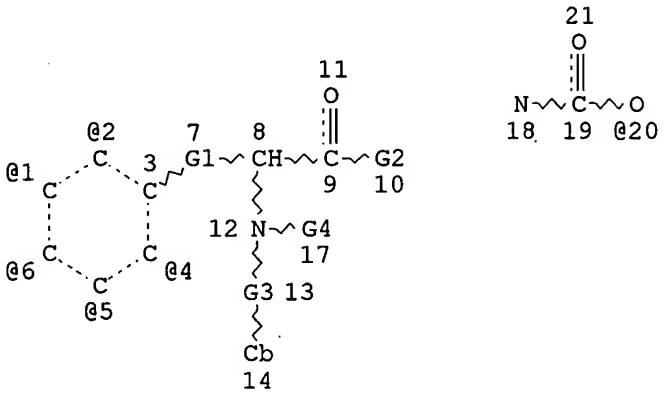


REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VPA 20-1/2/4/5/6 U

NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L17 STR



REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
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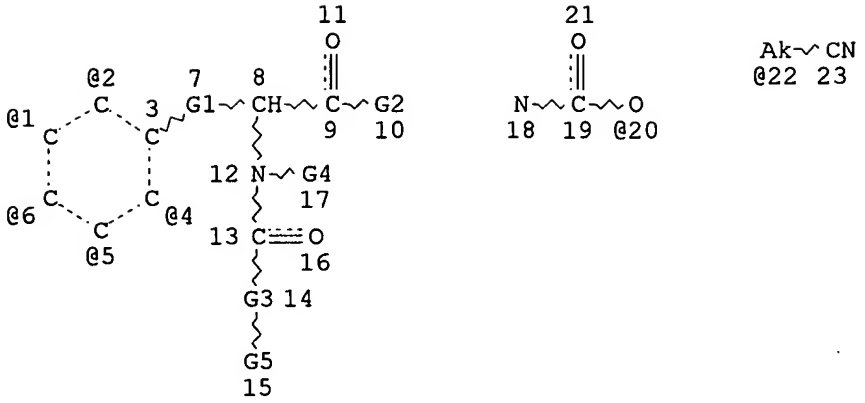
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L18 STR



REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/CY
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L19 541 SEA FILE=REGISTRY SSS FUL L15 OR L16 OR L17 OR L18
L20 171 SEA FILE=REGISTRY SUB=L19 SSS FUL (L11 OR L12 OR L13 OR L14)

100.0% PROCESSED 539 ITERATIONS 171 ANSWERS
SEARCH TIME: 00.00.02

FILE 'CAPLUS' ENTERED AT 10:55:49 ON 26 APR 2005
L21 14 S L20
L22 0 S L21 NOT (PY=>1999 OR PD=>19990924)

E1 THROUGH E171 ASSIGNED

L21 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 25 Mar 2005
ACCESSION NUMBER: 2005:260065 CAPLUS
DOCUMENT NUMBER: 142:316825
TITLE: Preparation of dioxolane derivatives as cell adhesion inhibitors with therapeutic uses
INVENTOR(S): Palle, Venkata P.; Sattigeri, Viswajanani J.; Salman, Mohammad; Soni, Ajay; Ray, Abhijit; Dastidar, Sunanda G.
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

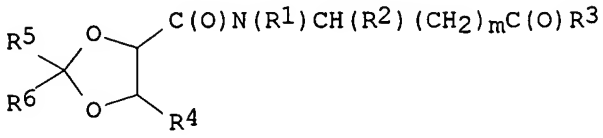
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005026163	A1	20050324	WO 2004-IB3047	20040917

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

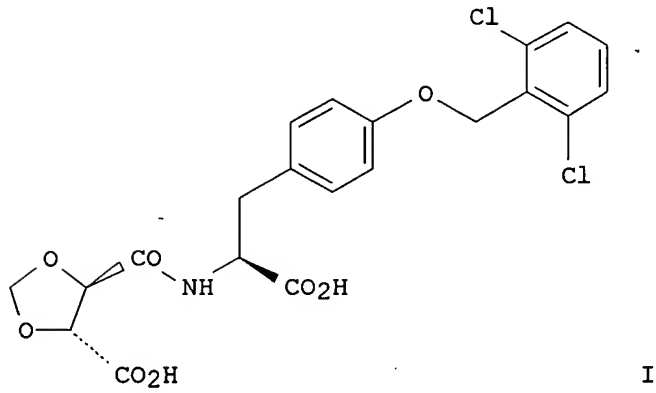
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-503643P P 20030917

GI



I



II

AB The present invention relates to dioxolane derivs. (shown as I; variables defined below; e.g. (4R,5R)-5-[[(S)-1-carboxy-2-[4-(2,6-dichlorobenzyloxy)phenyl]ethyl]carbamoyl]-[1,3]dioxolane-4-carboxylic acid (shown as II)), their pharmaceutically acceptable salts, pharmaceutically acceptable solvates, enantiomers, diastereomers, polymorphs or N-oxides as cell adhesion inhibitors (no data). These compds. can be useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies, including inflammatory and autoimmune diseases such as bronchial asthma, rheumatoid arthritis, type I diabetes, multiple sclerosis, allograft rejection or psoriasis. This invention also relates to pharmacol. compns. containing the compds. of the present invention, and the methods of treating bronchial

asthma, rheumatoid arthritis, multiple sclerosis, type I diabetes, psoriasis, allograft rejection, and other inflammatory and/or autoimmune disorders, using the compds. For I: m = 0-2; R1 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroarylalkyl, or heterocyclylalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, carboxy, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; R1 and R2 may together join to form a cyclic ring (3-8 membered), which may be optionally benzo-fused, containing 0-4 heteroatoms such as O, S, or N, wherein the rings may be substituted with ≥1 alkyl, alkenyl, alkynyl, (un)substituted amino, cycloalkyl, carboxy, alkoxy, aryloxy, halogen, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl or heterocyclylalkyl. R3 = NH2, NHOH, NHOR (R = alkyl, alkenyl, alkynyl, cycloalkyl or aralkyl), or ORm (Rm = H, alkyl, aralkyl, aryl, or metal ions (Na, K, Li, Ca or Mg)); R4 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, -(CH2)1-4-OR' (R'= H, alkyl, alkenyl, alkynyl, aralkyl, aryl, heterocyclylalkyl, or heteroarylalkyl), -C(O)R3, -C(O)Rz (Rz is -NR7R8, R7 and R8 = H (provided that both R7 and R8 are not H, represented as amino), alkyl, alkenyl, alkynyl, aralkyl, cycloalkyl, hydroxyalkyl, aralkyloxy, aryl, heteroaryl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, SO2R9 (R9 = alkyl, alkenyl, alkynyl, cycloalkyl, aralkyl, aryl, heterocyclyl, heteroaryl, heteroarylalkyl, heterocyclylalkyl)). Or R7 and R5 may together join to form a cyclic ring (3-8 membered), which may be optionally benzo-fused, containing 0-4 heteroatoms such as O, S, or N, wherein the rings may be substituted with ≥1 of alkyl, alkenyl, alkynyl, (un)substituted amino, cycloalkyl, carboxy, alkoxy, hydroxy, oxo, aryloxy, aryl, halogen, aralkyl, heteroaryl, heterocyclyl, heteroarylalkyl, or heterocyclylalkyl; or (CH2)1-4NRxRy (Rx and Ry = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl, -YRu (Y is C(O), C(S) or SO2 and Ru is alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heterocyclyl, heterocyclylalkyl or heteroarylalkyl), -C(:T)NRu (T is O, S, -CH(NO2), -N(NO2) or -N(CN)) or -C(O)ORu); R5 and R6 = H, alkyl, cycloalkyl, heterocyclyl, heteroarylalkyl, heterocyclylalkyl, aryl, or aralkyl; or R5 and R6 may together join to form a cycloalkyl ring. Methods of preparation of I and intermediates are claimed and 14 example prepns. are included. For example, II was prepared in 4 steps starting from di-Et (4R,5R)-[1,3]dioxolane-4,5-dicarboxylate and involving intermediates (4R,5R)-[1,3]dioxolane-4,5-dicarboxylic acid monoethyl ester, (4R,5R)-5-[[(S)-1-(benzyloxycarbonyl)-2-(4-hydroxyphenyl)ethyl]carbamoyl]-[1,3]dioxolane-4-carboxylic acid Et ester, and (4R,5R)-5-[[(S)-1-(benzyloxycarbonyl)-2-[4-(2,6-dichlorobenzyloxy)phenyl]ethyl]carbamoyl]-[1,3]dioxolane-4-carboxylic acid Et ester.

IT **848209-78-9P**, 4-Methylpiperazine-1-carboxylic acid 4-[(S)-2-[[[(4R,5R)-5-(biphenyl-2-ylcarbamoyl)-[1,3]dioxolan-4-yl]carbonyl]amino]-2-carboxyethyl]phenyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of dioxolane derivs. as cell adhesion inhibitors with therapeutic uses)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 07 Jan 2005
ACCESSION NUMBER: 2005:14169 CAPLUS
DOCUMENT NUMBER: 142:114470
TITLE: Preparation of sulfonylated peptide derivatives for treating rheumatoid arthritis
INVENTOR(S): Yednock, Theodore A.; Freedman, Stephen B.; Lieberburg, Ivan; Pleiss, Michael A.; Konradi, Andrei W.; Shopp, George; Messersmith, Elizabeth
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 736 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000246	A2	20050106	WO 2004-US20280	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005065192	A1	20050324	US 2004-875282	20040625
US 2005074451	A1	20050407	US 2004-875469	20040625
PRIORITY APPLN. INFO.:			US 2003-482211P P	20030625

OTHER SOURCE(S): MARPAT 142:114470

AB The invention relates to methods and compns. for treating rheumatoid arthritis by administering a combination therapy comprising methotrexate and an antibody to α4 integrin or an immunol. active antigen binding fragment in therapeutically effective amts. Compds. R1SO2NR2CHR3-Q-CHR5CO2H [R1 is (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl or heteroaryl; R2 is H, (un)substituted cycloalkenyl or any group given for R1; R3 is H or any group given for R1; R2 can combine with R1 or R3 to form an (un)substituted heterocyclic group; R5 is -(CH2)1-4-Ar-R5', where R5' is -O-Z-NR8R8' or -O-Z-R8'', Ar is (un)substituted aryl or heteroaryl, Z is CO or SO2, R8, R8' are H, (un)substituted alkyl, cycloalkyl or heterocyclyl or NR8R8' is (un)substituted heterocyclyl, and R8'' is (un)substituted heterocyclyl; Q is -C(X)NR7-, where R7 is H or alkyl and X is O or S] are claimed for use in combination therapy. Thus, N-tosyl-L-prolyl-4-(dimethylcarbamoyloxy)-L-phenylalanine Et ester was prepared by acylation of Ts-Pro-Tyr-OEt with dimethylcarbamoyl chloride. Compds. of the invention have binding affinity to α4β1 (IC50 ≤ 15 μM).

IT **220544-38-7P 220546-84-9P 220546-92-9P 821800-09-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)

IT **220543-91-9P 220543-93-1P 220543-94-2P**
220543-95-3P 220544-06-9P 220544-07-0P
220544-36-5P 220544-39-8P 220544-62-7P
220544-82-1P 220544-83-2P 220544-87-6P
220545-06-2P 220545-11-9P 220545-12-0P
220545-13-1P 220545-14-2P 220545-15-3P
220545-17-5P 220545-21-1P 220545-28-8P
220545-29-9P 220545-30-2P 220545-31-3P
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220546-54-3P 220546-60-1P 220546-71-4P
220546-77-0P 220546-79-2P 220546-80-5P
220546-85-0P 220546-87-2P 220546-96-3P
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821800-42-4P 821800-43-5P 821800-44-6P
821800-45-7P 821800-46-8P 821800-47-9P
821800-48-0P 821800-49-1P 821800-50-4P
821800-51-5P 821800-52-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)

IT **220548-09-4 821800-18-4 821800-19-5**
821800-20-8 821800-21-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)

L21 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 07 Jan 2005
ACCESSION NUMBER: 2005:14167 CAPLUS
DOCUMENT NUMBER: 142:114469
TITLE: Preparation of sulfonylated peptide derivatives for treating rheumatoid arthritis
INVENTOR(S): Yednock, Theodore A.; Freedman, Stephen B.; Lieberburg, Ivan; Pleiss, Michael A.; Konradi, Andrei W.; Shopp, George; Messersmith, Elizabeth
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 647 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000244	A2	20050106	WO 2004-US20240	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005065192	A1	20050324	US 2004-875282	20040625
US 2005074451	A1	20050407	US 2004-875469	20040625
PRIORITY APPLN. INFO.:			US 2003-482211P P	20030625

AB The invention relates to methods and compns. for treating rheumatoid arthritis by administering a combination therapy comprising methotrexate and an antibody to α4 integrin or an immunol. active antigen binding fragment in therapeutically effective amts. Compds. include those described by formula R1SO2NR2CHR3-Q-CHR5CO2H [R1 is (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl or heteroaryl; R2 is H, (un)substituted cycloalkenyl or any group given for R1; R3 is H or any group given for R1; R2 can combine with R1 or R3 to form an (un)substituted heterocyclic group; R5 is -(CH2)1-4-Ar-R5', where R5' is -O-Z-NR8R8' or -O-Z-R8'', Ar is (un)substituted aryl or heteroaryl, Z is CO or SO2, R8, R8' are H, (un)substituted alkyl, cycloalkyl or heterocyclyl or NR8R8' is (un)substituted heterocyclyl, and R8'' is (un)substituted heterocyclyl; Q is -C(X)NR7-, where R7 is H or alkyl and X is O or S]. Thus, N-tosyl-L-prolyl-4-(dimethylcarbamoyloxy)-L-phenylalanine Et ester was prepared by acylation of Ts-Pro-Tyr-OEt with dimethylcarbamoyl chloride. Compds. of the invention have binding affinity to α4β1 (IC50 ≤ 15 μM).

IT **220544-38-7P 220546-84-9P 220546-92-9P 821800-09-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)

IT **220543-91-9P 220543-93-1P 220543-94-2P 220543-95-3P 220544-06-9P 220544-07-0P 220544-36-5P 220544-39-8P 220544-62-7P 220545-28-8P 220545-29-9P 220545-30-2P 220545-31-3P 220545-32-4P 220545-35-7P 220545-43-7P 220546-54-3P 220546-60-1P 220546-71-4P 220546-77-0P 220546-79-2P 220546-80-5P 220546-85-0P 220546-87-2P 220546-96-3P 220547-10-4P 220547-27-3P 220547-28-4P 220547-44-4P 220547-50-2P 737799-24-5P 737799-44-9P 821800-08-2P 821800-10-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)
IT **220548-09-4 821800-18-4 821800-19-5 821800-20-8 821800-21-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonylated peptide derivs. for treating rheumatoid arthritis)

L21 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 06 Oct 2004
ACCESSION NUMBER: 2004:812749 CAPLUS
DOCUMENT NUMBER: 142:48474
TITLE: The identification and optimization of orally efficacious, small molecule VLA-4 antagonists
AUTHOR(S): Huryn, Donna M.; Konradi, Andrei W.; Ashwell, Susan; Freedman, Stephen B.; Lombardo, Louis J.; Pleiss, Michael A.; Thorsett, Eugene D.; Yednock, Ted; Kennedy, Jeffrey D.
CORPORATE SOURCE: Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2004), 4(14), 1473-1484
CODEN: CTMCCL; ISSN: 1568-0266
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The identification of orally active, small mol. antagonists of the α4β1 integrin, VLA-4, could lead to therapeutic agents with utility in a number of clin. settings, including asthma, multiple sclerosis and IBD. Starting from CDR3 sequences conserved among neutralizing α4 antibodies, peptides were identified that antagonized VLA-4 mediated adhesion in vitro. Through a series of structural modifications, these peptides evolved into small mols. that exhibited high potency and selectivity for VLA-4 in cell adhesion assays. Finally, through the optimization of phys. and pharmacokinetic properties, compds. were identified that exhibited oral activity in animal models of asthma and multiple sclerosis.
IT **220543-95-3**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(identification and optimization of orally efficacious, small mol. VLA-4 antagonists)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 Aug 2004
ACCESSION NUMBER: 2004:648332 CAPLUS
DOCUMENT NUMBER: 141:191071
TITLE: Preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis
INVENTOR(S): Karlik, Steve J.; Pleiss, Michael A.; Konradi, Andrei W.; Grant, Francine S.; Semko, Christopher M.; Dressen, Daren; Messersmith, Elizabeth; Freedman, Stephen; Yednock, Ted
PATENT ASSIGNEE(S): Elan Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 495 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004066932	A2	20040812	WO 2004-US2039		20040126
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
US 2005069541	A1	20050331	US 2004-763424		20040126
PRIORITY APPLN. INFO.:			US 2003-442171P	P	20030124
			US 2003-500316P	P	20030905

AB The application provides for methods and compns. for inhibiting demyelination, promoting remyelination and/or treating paralysis. Preferably, the compns. include Igs (e.g., antibodies, antibody fragments, and recombinantly produced antibodies or fragments), polypeptides (e.g., soluble forms of the ligand proteins for integrins) and small mols., which when administered in an effective amount inhibit demyelination and/or promote remyelination. The compns. can also utilize other anti-inflammatory agents used to palliate conditions and diseases associated with demyelination. Compds. of the invention include sulfonyl dipeptides R1SO2NR2CHR3-Q-CHR5CO2H [R1 is (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl or heteroaryl; R2 is H, (un)substituted cycloalkenyl or any group given for R1; R3 is H or any group given for R1; R1 and R2 or R2 and R3 can form an (un)substituted heterocyclic group; R5 is -(CH2)0-4-Ar-R5', where R5' is -O-Z-NR8R8' or -O-Z-R8'' [R8, R8'' are H, (un)substituted alkyl, cycloalkyl or heterocyclyl or form a heterocycle, R8'' is (un)substituted heterocyclyl, Z is CO or SO2 and Ar is (un)substituted aryl or heteroaryl]; Q is C(X)NR7, where R7 is H or alkyl and X is O or S] or their pharmaceutically-acceptable salts. The examples describe synthetic data and specific compds. of the invention (approx. 300) which were prepared Thus, claimed compound N-[N-(3-pyridinesulfonyl)-L-3,3-dimethyl-4-thiaprolyl]-O-[1-methylpiperazin-4-ylcarbonyl]-L-tyrosine iso-Pr ester was prepared by a peptide coupling/sulfonylation/acylation scheme and assayed for biol. activity, e.g., reversal of prolonged chronic exptl. autoimmune encephalomyelitis.

IT **220544-38-7P 220546-92-9P 220547-27-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

IT **220543-91-9P 220543-93-1P 220543-94-2P**
220543-95-3P 220544-06-9P 220544-07-0P
220544-36-5P 220544-39-8P 220544-62-7P
220545-28-8P 220545-29-9P 220545-30-2P
220545-31-3P 220545-32-4P 220545-35-7P
220545-43-7P 220546-54-3P 220546-60-1P
220546-71-4P 220546-77-0P 220546-79-2P

220546-80-5P 220546-84-9P 220546-85-0P
220546-87-2P 220546-96-3P 220547-10-4P
220547-28-4P 220547-44-4P 220547-50-2P
737799-24-5P 737799-44-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

IT **220548-09-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

L21 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 Aug 2004
ACCESSION NUMBER: 2004:648331 CAPLUS
DOCUMENT NUMBER: 141:191070
TITLE: Preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis
INVENTOR(S): Karlik, Steve J.; Pleiss, Michael A.; Konradi, Andrei W.; Grant, Francine S.; Semko, Christopher M.; Dressen, Daren; Messersmith, Elizabeth; Freedman, Stephen; Yednock, Ted
PATENT ASSIGNEE(S): Elan Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 573 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004066931	A2	20040812	WO 2004-US2028		20040126
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
US 2005069541	A1	20050331	US 2004-763424		20040126
PRIORITY APPLN. INFO.:			US 2003-442171P	P	20030124
			US 2003-500316P	P	20030905

OTHER SOURCE(S): MARPAT 141:191070
AB The application provides for methods and compns. for inhibiting demyelination, promoting remyelination and/or treating paralysis. Preferably, the compns. include Igs (e.g., antibodies, antibody fragments, and recombinantly produced antibodies or fragments), polypeptides (e.g., soluble forms of the ligand proteins for integrins) and small mols., which when administered in an effective amount inhibit demyelination and/or promote remyelination. The compns. can also utilize other anti-inflammatory agents used to palliate conditions and diseases associated with demyelination. The claims describe sulfonyl dipeptides R1SO2NR2CHR3-Q-CHR5CO2H [R1 is (un)substituted alkyl, aryl, cycloalkyl, heterocyclyl or heteroaryl; R2 is H, (un)substituted

cycloalkenyl or any group given for R1; R3 is H or any group given for R1; or R1 and R2 or R2 and R3 can form an (un)substituted heterocyclic group; R5 is -(CH2)0-4-Ar-R5', where R5' is -O-Z-NR8R8' or -O-Z-R8'' [R8, R8'' are H, r3 is (un)substituted alkyl, cycloalkyl or heterocyclyl or form a heterocycle, R8'' is (un)substituted heterocyclyl, Z is CO or SO2 and Ar is (un)substituted aryl or heteroaryl]; Q is C(X)NR7, where R7 is H or alkyl and X is O or S] or their pharmaceutically-acceptable salts for treating demyelinating diseases. The examples describe synthetic data and specific compds. of the invention (approx. 300) which were prepared Thus, claimed compound N-[N-(3-pyridinesulfonyl)-L-3,3-dimethyl-4-thiaprolyl]-O-[1-methylpiperazin-4-ylcarbonyl]-L-tyrosine iso-Pr ester was prepared by a peptide coupling/sulfonylation/acylation scheme and assayed for biol. activity, e.g., reversal of prolonged chronic exptl. autoimmune encephalomyelitis.

IT **220544-38-7P 220545-12-0P 220545-14-2P**
220545-15-3P 220546-92-9P 220547-27-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

IT **220543-91-9P 220543-93-1P 220543-94-2P**
220543-95-3P 220544-06-9P 220544-07-0P
220544-36-5P 220544-39-8P 220544-62-7P
220544-82-1P 220544-83-2P 220544-87-6P
220545-06-2P 220545-11-9P 220545-13-1P
220545-17-5P 220545-21-1P 220545-28-8P
220545-29-9P 220545-30-2P 220545-31-3P
220545-32-4P 220545-35-7P 220545-43-7P
220546-54-3P 220546-60-1P 220546-71-4P
220546-77-0P 220546-79-2P 220546-80-5P
220546-84-9P 220546-85-0P 220546-87-2P
220546-96-3P 220547-10-4P 220547-28-4P
220547-34-2P 220547-35-3P 220547-38-6P
220547-44-4P 220547-45-5P 220547-46-6P
220547-50-2P 220547-52-4P 220547-54-6P
220547-55-7P 220547-61-5P 220547-66-0P
220547-67-1P 220547-68-2P 220547-69-3P
220547-70-6P 220547-71-7P 220547-72-8P
220547-76-2P 220547-77-3P 220547-78-4P
220547-79-5P 220547-80-8P 220547-83-1P
220547-84-2P 220547-85-3P 220547-86-4P
220547-87-5P 220547-88-6P 220547-91-1P
220547-92-2P 220547-93-3P 737799-24-5P
737799-44-9P 738614-05-6P 738614-06-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

IT **220548-09-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of sulfonyl dipeptides for treatment of demyelinating diseases and paralysis)

L21 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 27 Sep 2002
ACCESSION NUMBER: 2002:732382 CAPLUS

DOCUMENT NUMBER: 138:313904
TITLE: Solid-phase synthesis of dual α4β1/α4β7 integrin antagonists: two scaffolds with overlapping pharmacophores
AUTHOR(S): Castanedo, Georgette M.; Sailes, Fredrick C.; Dubree, Nathan J. P.; Nicholas, John B.; Caris, Lisa; Clark, Kevin; Keating, Susan M.; Beresini, Maureen H.; Chiu, Henry; Fong, Sherman; Marsters, James C.; Jackson, David Y.; Sutherlin, Daniel P.
CORPORATE SOURCE: Department of Bioorganic Chemistry, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2913-2917
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:313904
AB Two structural classes of dual α4β1/α4β7 integrin antagonists were investigated via solid-phase parallel synthesis. Using an acylated amino acid backbone, lead compds. containing biphenylalanine or tyrosine carbamate scaffolds were optimized for inhibition of α4β1/VCAM and α4β7/MAdCAM. A comparison of the structure-activity relationships in the inhibition of the α4β7/MAdCAM interaction for substituted amines employed in both scaffolds suggests a similar binding mode for the compds.
IT **331469-49-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of dual α4β1/α4β7 integrin antagonists)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 30 Mar 2001
ACCESSION NUMBER: 2001:228855 CAPLUS
DOCUMENT NUMBER: 134:252658
TITLE: Preparation of tyrosine derivatives as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.
INVENTOR(S): Jackson, David Y.; Sailes, Frederick C.; Sutherlin, Daniel P.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021584	A1	20010329	WO 2000-US26326	20000925

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2385882	AA	20010329	CA 2000-2385882	20000925
EP 1214292	A1	20020619	EP 2000-965417	20000925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6469047	B1	20021022	US 2000-669779	20000925
JP 2003509488	T2	20030311	JP 2001-524964	20000925
US 2004110753	A1	20040610	US 2002-198328	20020716
US 2004158076	A1	20040812	US 2004-772678	20040204
PRIORITY APPLN. INFO.:			US 1999-156062P	P 19990924
			US 2000-669779	A1 20000925
			WO 2000-US26326	W 20000925
			US 2002-198328	A1 20020716

OTHER SOURCE(S): MARPAT 134:252658

AB Tyrosine derivs., e.g., ArCH2CH[N(A)(Z)]CO-Y [Z = H, alkyl; A = B(CH2)q-X-, where B = (un)substituted Ph and X = CO, SO2, null or B = cyanoalkyl, carbocyclyl or heterocyclyl and X = CO; R6 = H, alkyl, amino, cyano, hydroxy, alkylsulfonyl, etc.; q = 0-3; Y is H, (un)substituted alkoxy, alkoxyalkoxy, aryloxy, alkylaminoalkoxy, dialkylaminoalkoxy,alkylamino, arylamino, heterocyclyl or heteroarylalkyl; Ar is Ph which has hydroxy, carbonate, thiocarbonate, carbamoyloxy or acyloxy groups and optionally other substituents] were prepared as inhibitors of α4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM. Methods of synthesis are described and inhibitory binding data are tabulated for 416 compds., including N-(o-chlorobenzoyl)-O-(allylcarbamoyl)-L-tyrosine, for which IC50 is < 1.0 micromolar.

IT **331468-18-9P 331468-26-9P 331468-27-0P**
331468-28-1P 331468-29-2P 331468-30-5P
331468-31-6P 331468-32-7P 331468-35-0P
331468-38-3P 331468-39-4P 331469-12-6P
331469-13-7P 331469-16-0P 331469-40-0P
331469-41-1P 331469-46-6P 331469-49-9P
331469-50-2P 331469-51-3P 331469-52-4P
331469-75-1P 331469-76-2P 331469-77-3P
331469-80-8P 331469-81-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.)

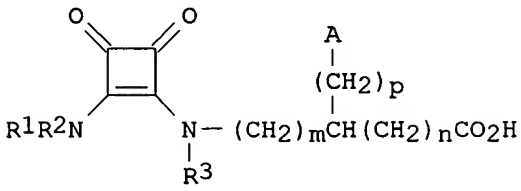
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN

ED Entered STN: 28 Dec 2000
ACCESSION NUMBER: 2000:909217 CAPLUS
DOCUMENT NUMBER: 134:56962
TITLE: Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Lombardo, Louis J.; Sabalski, Joan
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6166050	A	20001226	US 1999-458852		19991210
PRIORITY APPLN. INFO.:			US 1998-155221P	P	19981214

OTHER SOURCE(S): MARPAT 134:56962
GI



I

AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 = 58 μM for binding of α4β1 integrin (VLA-4).

IT **274927-51-4P 274927-53-6P 274927-56-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

IT **274927-49-0P 274927-50-3P 274927-52-5P 274927-54-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L21 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 28 Jul 2000
ACCESSION NUMBER: 2000:513715 CAPLUS
DOCUMENT NUMBER: 133:129864
TITLE: Pyroglutamic acid derivatives and related compounds which inhibit leukocyte adhesion mediated by VLA-4, and preparation thereof
INVENTOR(S): Dressen, Darren B.; Kreft, Anthony; Kubrak, Dennis; Mann, Charles William; Pleiss, Michael A.; Stack, Gary Paul; Thorsett, Eugene D.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043413	A2	20000727	WO 2000-US1537	20000121
WO 2000043413	A3	20001130		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358093	AA	20000727	CA 2000-2358093	20000121
EP 1144435	A2	20011017	EP 2000-904486	20000121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6407066	B1	20020618	US 2000-489164	20000121
US 2003027771	A1	20030206	US 2002-139382	20020507

PRIORITY APPLN. INFO.:	US 1999-198244P	P	19990126
	US 1999-238661	A1	19990126
	US 2000-489164	A1	20000121
	WO 2000-US1537	W	20000121

OTHER SOURCE(S): MARPAT 133:129864

AB Pyroglutamic acid derivs. and related compds. that bind VLA-4 are disclosed. Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis, and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

IT **286456-37-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(pyroglutamic acid derivs. and related compds. which inhibit VLA-4-mediated leukocyte adhesion, and preparation thereof)

IT **286456-28-8P 286456-29-9P 286456-33-5P**
286456-34-6P 286456-38-0P 286456-62-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyroglutamic acid derivs. and related compds. which inhibit VLA-4-mediated leukocyte adhesion, and preparation thereof)

IT **286456-72-2 286457-63-4 286457-64-5**
286457-65-6 286457-66-7 286457-67-8
286457-68-9 286458-22-8 286458-23-9
286458-24-0 286458-25-1 286458-26-2
286458-27-3 286458-28-4 286458-50-2
286458-51-3 286458-52-4 286458-53-5
286458-54-6 286458-55-7 286458-56-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyroglutamic acid derivs. and related compds. which inhibit VLA-4-mediated leukocyte adhesion, and preparation thereof)

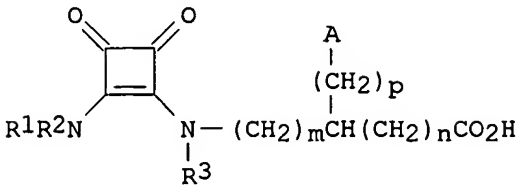
L21 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 23 Jun 2000
ACCESSION NUMBER: 2000:421084 CAPLUS
DOCUMENT NUMBER: 133:43808
TITLE: Preparation of 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Lombardo, Louis John; Sabalski, Joan E.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035855	A1	20000622	WO 1999-US29369	19991210
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2351464	AA	20000622	CA 1999-2351464	19991210
BR 9916211	A	20010911	BR 1999-16211	19991210
EP 1140792	A1	20011010	EP 1999-967265	19991210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1998-211183 A 19981214

WO 1999-US29369 W 19991210

OTHER SOURCE(S): MARPAT 133:43808
GI



I

AB Diaminocyclobutenedione amino acid derivs. I (R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or R1R2N form a saturated or unsatd. heterocyclic ring; R3 = H, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; A = aryl, heteroaryl; m, n, p = 0-3) were prepared for the treatment of inflammatory and autoimmune diseases. Thus, N-[2-(benzylamino)-3,4-dioxocyclobut-1-enyl]-L-phenylalanine, prepared by treatment of L-phenylalanine Me ester hydrochloride with 3,4-diethoxy-3-cyclobutene-1,2-dione and benzylamine and saponification, showed IC50 for binding of the α4β1 integrin (VLA-4).

IT **274927-51-4P 274927-53-6P 274927-56-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

IT **274927-49-0P 274927-50-3P 274927-52-5P 274927-54-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of diaminocyclobutenedione derivs. which inhibit leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Feb 1999
ACCESSION NUMBER: 1999:113710 CAPLUS
DOCUMENT NUMBER: 130:153984
TITLE: Preparation of N-sulfonyl dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Pleiss, Michael A.; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.; Baudy, Reinhardt Bernhard
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation

SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906435	A1	19990211	WO 1998-US15314	19980730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2291475	AA	19990211	CA 1998-2291475	19980730
AU 9886612	A1	19990222	AU 1998-86612	19980730
EP 994895	A1	20000426	EP 1998-937991	19980730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 9806834	A	20000502	ZA 1998-6834	19980730
BR 9811599	A	20000919	BR 1998-11599	19980730
JP 2001512137	T2	20010821	JP 2000-505190	19980730
NO 2000000412	A	20000324	NO 2000-412	20000127
PRIORITY APPLN. INFO.:			US 1997-904415 A1	19970731
			WO 1998-US15314 W	19980730

OTHER SOURCE(S): MARPAT 130:153984

AB Disclosed are title compds. R1SO2NR2CR3R4QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1, (un)substituted cycloalkenyl; R1R2 may form heterocyclic ring; R3 = any group R1; R2R3 may form heterocyclic ring; R4 = any group R1; R3R4 may form cycloalkyl, (un)substituted heterocyclic ring; R5 = CHMe2, CH2X, :CHX1; X1 = H, OH, acylamino, optionally substituted alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxy, carboxyalkyl, etc.; Q = C(X)NR7, X = O, S, R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, β-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z; R11 = alkyl; Z = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin α4β1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, sulfonylation of

cycloleucine (1-aminocyclopentanecarboxylic acid) with tosyl chloride, followed by peptide coupling with L-phenylalanine Me ester and saponification
gave desired title compound 4-MeC6H4SO2-cycloleucyl-L-phenylalanine.

IT **220173-39-7P 220173-41-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-sulfonyl dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Feb 1999
ACCESSION NUMBER: 1999:113667 CAPLUS
DOCUMENT NUMBER: 130:177528
TITLE: α9-Integrin antagonists and anti-inflammatory compositions
INVENTOR(S): Yednock, Theodore A.; Pleiss, Michael A.
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906391	A1	19990211	WO 1998-US15958	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9806830	A	20000502	ZA 1998-6830	19980730
CA 2267175	AA	19990211	CA 1998-2267175	19980731
AU 9886050	A1	19990222	AU 1998-86050	19980731
EP 954519	A1	19991110	EP 1998-937310	19980731
EP 954519	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001502361	T2	20010220	JP 1999-511273	19980731
US 2002039745	A1	20020404	US 1998-127364	19980731
US 6489300	B1	20021203	US 1998-126958	19980731
AT 236146	E	20030415	AT 1998-937310	19980731
TW 533211	B	20030521	TW 1998-87112594	19980731
CN 1119340	B	20030827	CN 1998-807770	19980731
EP 1452532	A1	20040901	EP 2004-11786	19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2221183	T3	20041216	ES 1998-937052	19980731

US 2002193312	A1	20021219	US 2001-987619	20011115
US 2003017993	A1	20030123	US 2001-987900	20011116
US 6525026	B2	20030225		
US 2004014677	A1	20040122	US 2002-316205	20021211
PRIORITY APPLN. INFO.:			US 1997-904424	A 19970731
			US 1997-54453P	P 19970801
			US 1997-112020P	P 19970731
			EP 1998-937052	A3 19980731
			US 1998-126958	A3 19980731
			WO 1998-US15958	W 19980731
			US 2001-987900	A3 20011116

OTHER SOURCE(S): MARPAT 130:177528

AB Pharmaceutical compns. and methods are provided for treating inflammatory conditions, particularly those that are characterized by increased binding of α9-integrin to one or more of its ligands. Also disclosed are methods for selecting compds. for use in such compns. and methods.

IT **220543-91-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; α9-integrin antagonists and anti-inflammatory compns.)

IT **220543-95-3 220545-11-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α9-integrin antagonists and anti-inflammatory compns.)

IT **220543-93-1P 220543-94-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(α9-integrin antagonists and anti-inflammatory compns.)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Feb 1999
ACCESSION NUMBER: 1999:113666 CAPLUS
DOCUMENT NUMBER: 130:182768
TITLE: Preparation of N-sulfonyl O-carbamoyltyrosine dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D.; Semko, Christopher M.; Sarantakis, Dimitrios; Pleiss, Michael A.; Kreft, Anthony; Konradi, Andrei W.; Grant, Francine S.; Dressen, Darren B.; Ashwell, Susan; Baudy, Reinhardt Bernhard; Lombardo, Louis John
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 386 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906390	A1	19990211	WO 1998-US15324	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9806830	A	20000502	ZA 1998-6830	19980730
CA 2290745	AA	19990211	CA 1998-2290745	19980731
AU 9885849	A1	19990222	AU 1998-85849	19980731
AU 740681	B2	20011108		
EP 1000051	A1	20000517	EP 1998-937052	19980731
EP 1000051	B1	20040519		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9811598	A	20001003	BR 1998-11598	19980731
JP 2001512114	T2	20010821	JP 2000-505149	19980731
US 2002039745	A1	20020404	US 1998-127364	19980731
US 6489300	B1	20021203	US 1998-126958	19980731
TW 533211	B	20030521	TW 1998-87112594	19980731
CN 1119340	B	20030827	CN 1998-807770	19980731
RU 2220964	C2	20040110	RU 2000-104850	19980731
AT 267188	E	20040615	AT 1998-937052	19980731
EP 1452532	A1	20040901	EP 2004-11786	19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2221183	T3	20041216	ES 1998-937052	19980731
NO 2000000413	A	20000328	NO 2000-413	20000127
US 2002193312	A1	20021219	US 2001-987619	20011115
US 2003017993	A1	20030123	US 2001-987900	20011116
US 6525026	B2	20030225		
US 2004014677	A1	20040122	US 2002-316205	20021211
PRIORITY APPLN. INFO.:			US 1997-904424	A1 19970731
			US 1997-54453P	P 19970801
			US 1997-112020P	P 19970731
			EP 1998-937052	A3 19980731
			US 1998-126958	A3 19980731
			WO 1998-US15324	W 19980731
			US 2001-987900	A3 20011116

OTHER SOURCE(S): MARPAT 130:182768

AB Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1; R1R2 may form (un)substituted heterocyclic ring; R3 = H, any group R1; R2R3

may form (un)substituted heterocyclic ring; R5 = (CH2)x-Ar-R5'; R5' = OZNR8R8', OZR12; R8, R8' = independently H, (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R12 = (un)substituted heterocyclyl; Z = CO, SO2; Ar = (un)substituted aryl or heteroaryl; x = 1-4; Q = C(X)NR7; R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, β-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z'; R11 = alkyl; Z' = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin α4β1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, carbamoylation of Ts-Pro-Tyr-OEt (Ts = tosyl) with Me2NCOCl in the presence of Et3N and DMAP gave 99% desired title compound Ts-Pro-Tyr(CONMe2)-OEt (I). Saponification of I gave the corresponding free acid Ts-Pro-Tyr(CONMe2)-OH. All prepared compds. have IC50 ≤ 15 μM in a VLA-4 binding assay.

IT **220543-91-9P 220544-06-9P 220544-38-7P**
220545-12-0P 220545-14-2P 220545-15-3P
220546-84-9P 220546-96-3P 220547-27-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

IT **220543-93-1P 220543-94-2P 220543-95-3P**
220544-07-0P 220544-36-5P 220544-39-8P
220544-62-7P 220544-82-1P 220544-83-2P
220544-87-6P 220545-06-2P 220545-11-9P
220545-13-1P 220545-17-5P 220545-21-1P
220545-28-8P 220545-29-9P 220545-30-2P
220545-31-3P 220545-32-4P 220545-35-7P
220545-43-7P 220546-54-3P 220546-60-1P
220546-71-4P 220546-77-0P 220546-79-2P
220546-80-5P 220546-85-0P 220546-87-2P
220546-92-9P 220547-10-4P 220547-28-4P
220547-34-2P 220547-35-3P 220547-38-6P
220547-44-4P 220547-45-5P 220547-46-6P
220547-50-2P 220547-51-3P 220547-52-4P
220547-53-5P 220547-54-6P 220547-55-7P
220547-61-5P 220547-66-0P 220547-67-1P
220547-68-2P 220547-69-3P 220547-70-6P
220547-71-7P 220547-72-8P 220547-76-2P
220547-77-3P 220547-78-4P 220547-79-5P
220547-80-8P 220547-83-1P 220547-84-2P
220547-85-3P 220547-86-4P 220547-87-5P
220547-88-6P 220547-91-1P 220547-92-2P
220547-93-3P 220547-94-4P 220547-95-5P

220547-96-6P 220547-99-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

IT **220548-09-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-sulfonyl O-carbamoyltyrosine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

FILE 'REGISTRY' ENTERED AT 10:57:08 ON 26 APR 2005

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Random RNs displayed ↓

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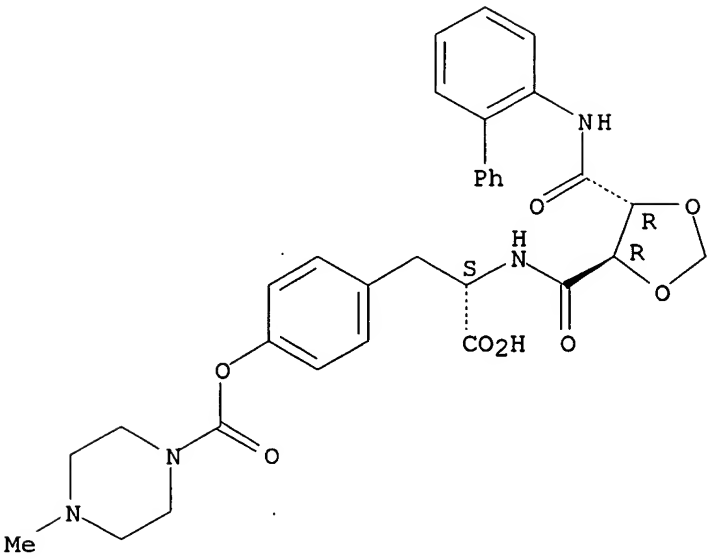
L23 ANSWER 1 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **848209-78-9** REGISTRY
ED Entered STN: 11 Apr 2005
CN L-Tyrosine, N-[[(4R,5R)-5-[([1,1'-biphenyl]-2-ylamino)carbonyl]-1,3-dioxolan-4-yl]carbonyl]-, 4-methyl-1-piperazinecarboxylate (ester)

(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H34 N4 O8
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



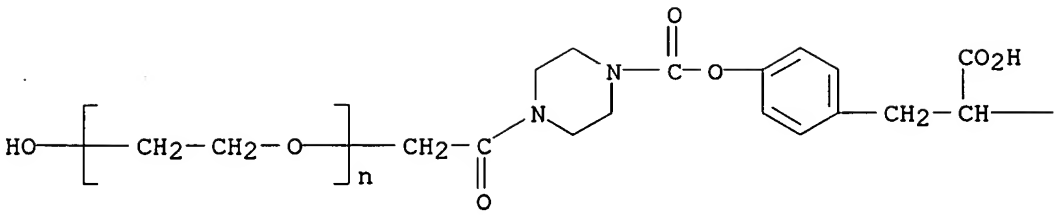
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:316825

L23 ANSWER 2 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **821800-52-6** REGISTRY
ED Entered STN: 28 Jan 2005
CN Poly(oxy-1,2-ethanediyl), α-[2-[4-[[4-[(2S)-2-carboxy-2-[[[(4R)-5,5-dimethyl-3-[(4-methylphenyl)sulfonyl]-4-thiazolidinyl]carbonyl]amino]ethyl]phenoxy]carbonyl]-1-piperazinyl]-2-oxoethyl]-ω-hydroxy- (9CI) (CA INDEX NAME)
MF (C2 H4 O)n C29 H36 N4 O9 S2
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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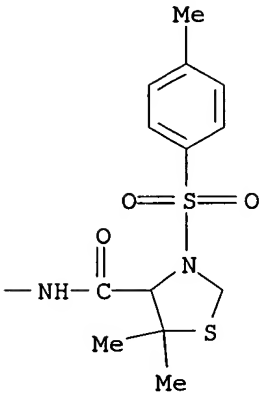
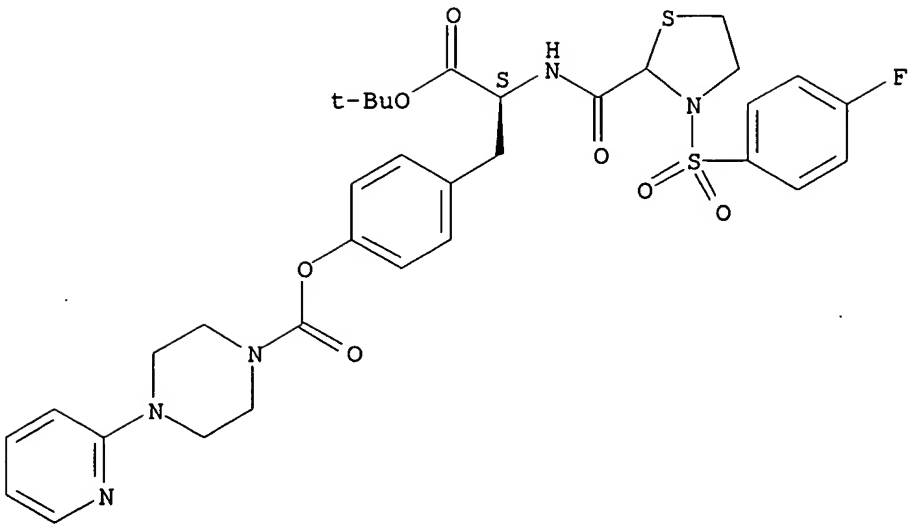


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

L23 ANSWER 24 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **738614-06-7** REGISTRY
ED Entered STN: 03 Sep 2004
CN 1-Piperazinecarboxylic acid, 4-(2-pyridinyl)-, 4-[(2S)-3-(1,1-dimethylethoxy)-2-[[[3-[(4-fluorophenyl)sulfonyl]-2-thiazolidinyl]carbonyl]amino]-3-oxopropyl]phenyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H38 F N5 O7 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



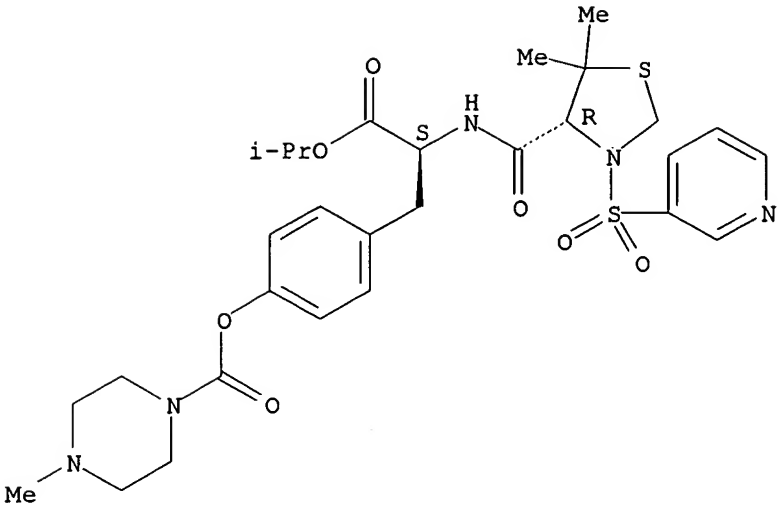
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:191070

L23 ANSWER 26 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **737799-44-9** REGISTRY
ED Entered STN: 02 Sep 2004
CN 1-Piperazinecarboxylic acid, 4-methyl-, 4-[(2S)-2-[[[(4R)-5,5-dimethyl-3-(3-pyridinylsulfonyl)-4-thiazolidinyl]carbonyl]amino]-3-(1-methylethoxy)-3-oxopropyl]phenyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H39 N5 O7 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

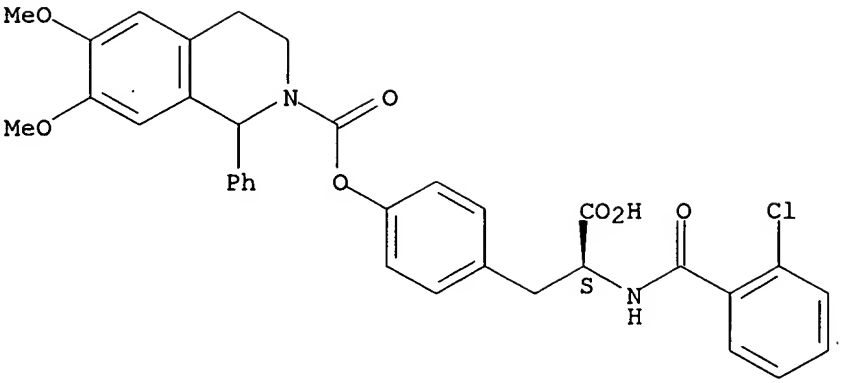
REFERENCE 2: 142:114469

REFERENCE 3: 141:191071

REFERENCE 4: 141:191070

L23 ANSWER 28 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **331469-81-9** REGISTRY
ED Entered STN: 16 Apr 2001
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-1-phenyl-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H31 Cl N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



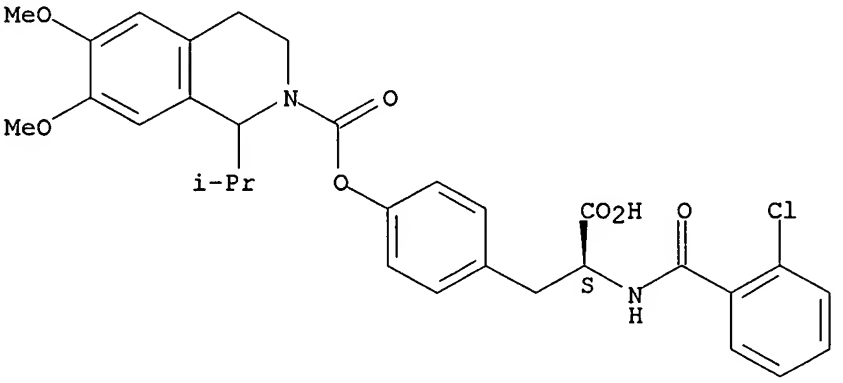
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:252658

L23 ANSWER 29 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **331469-80-8** REGISTRY
ED Entered STN: 16 Apr 2001
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-1-(1-methylethyl)-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H33 Cl N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



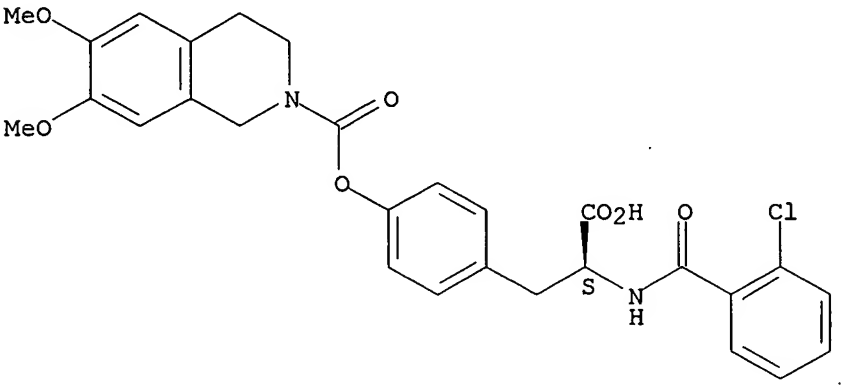
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:252658

L23 ANSWER 43 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **331468-39-4** REGISTRY
ED Entered STN: 16 Apr 2001
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H27 Cl N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



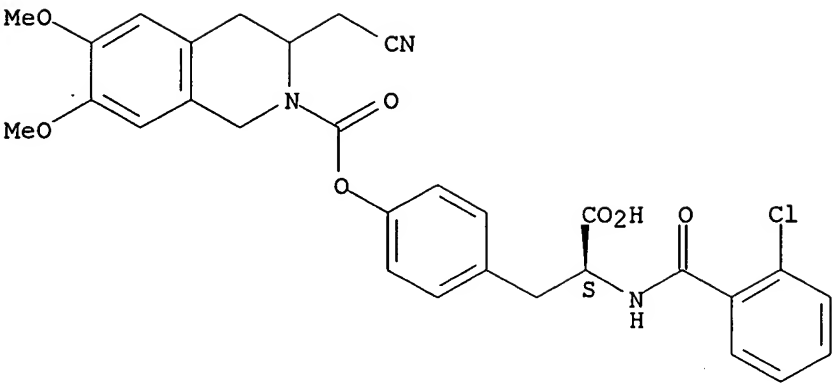
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:252658

L23 ANSWER 53 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **331468-18-9** REGISTRY
ED Entered STN: 16 Apr 2001
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3-(cyanomethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H28 Cl N3 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



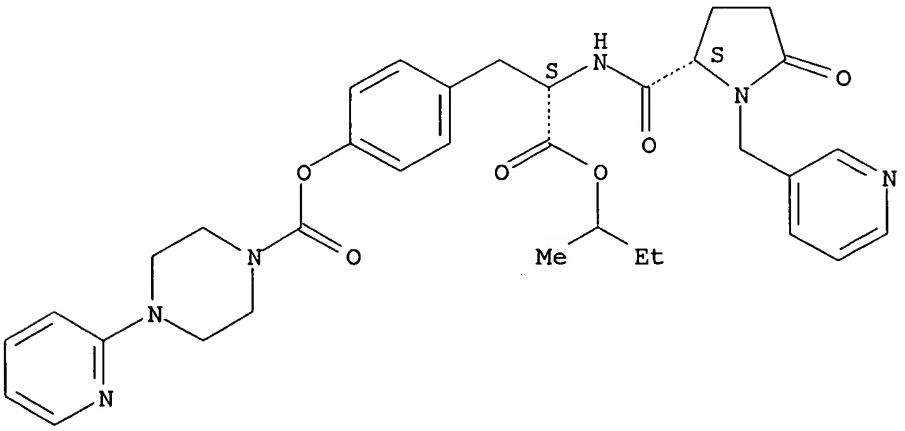
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:252658

L23 ANSWER 54 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **286458-56-8** REGISTRY
ED Entered STN: 18 Aug 2000
CN L-Tyrosine, 5-oxo-1-(3-pyridinylmethyl)-L-prolyl-, 1-methylpropyl ester, 4-(2-pyridinyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H40 N6 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

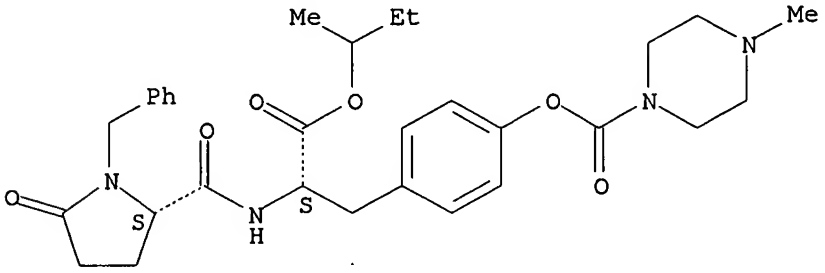
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searcher : Shears 571-272-2528

REFERENCE 1: 133:129864

L23 ANSWER 68 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **286457-68-9** REGISTRY
ED Entered STN: 18 Aug 2000
CN L-Tyrosine, 5-oxo-1-(phenylmethyl)-L-prolyl-, 1-methylpropyl ester, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H40 N4 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



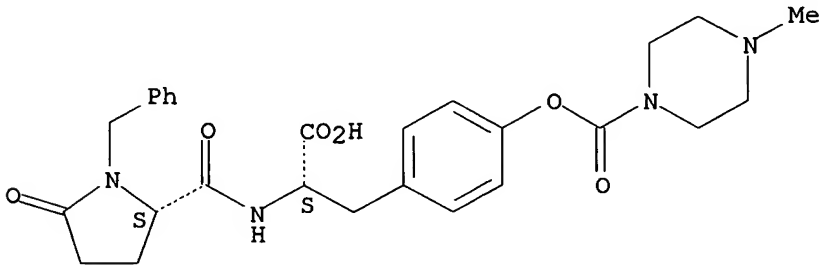
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:129864

L23 ANSWER 74 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **286456-72-2** REGISTRY
ED Entered STN: 18 Aug 2000
CN L-Tyrosine, 5-oxo-1-(phenylmethyl)-L-prolyl-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H32 N4 O6
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



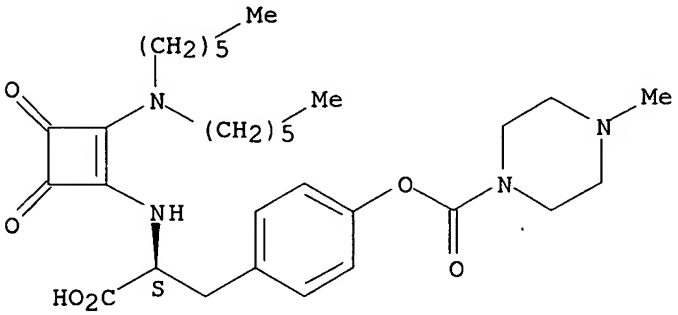
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:129864

L23 ANSWER 82 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **274927-56-9** REGISTRY
ED Entered STN: 06 Jul 2000
CN L-Tyrosine, N-[2-(dihexylamino)-3,4-dioxo-1-cyclobuten-1-yl]-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H46 N4 O6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



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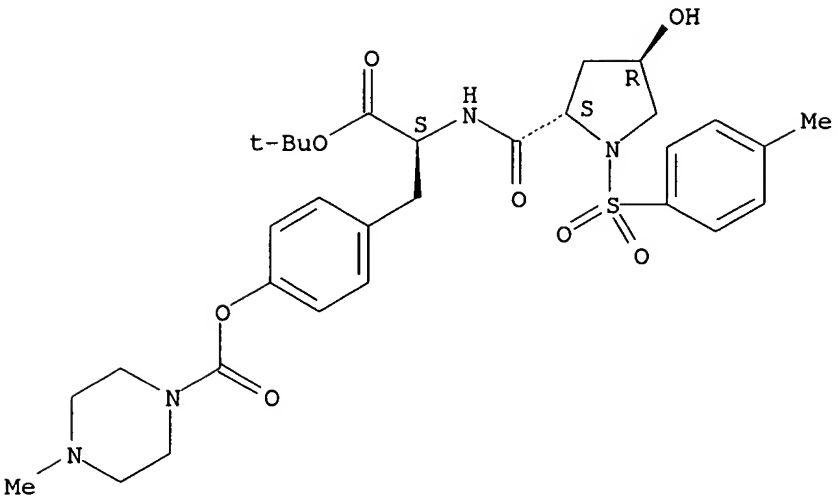
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:56962

REFERENCE 2: 133:43808

L23 ANSWER 89 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220548-09-4** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, (4R)-4-hydroxy-1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H42 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

REFERENCE 2: 142:114469

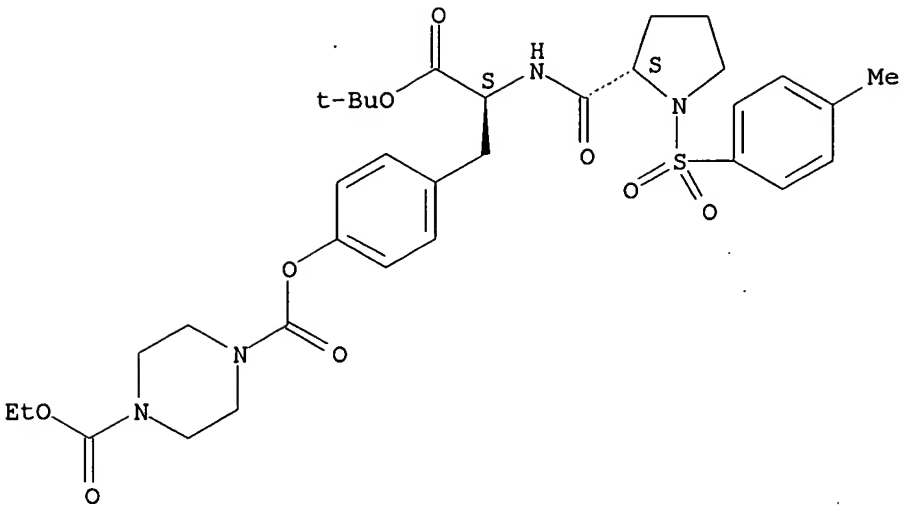
REFERENCE 3: 141:191071

REFERENCE 4: 141:191070

REFERENCE 5: 130:182768

L23 ANSWER 90 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220547-99-9** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, ethyl 1,4-piperazinedicarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H44 N4 O9 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

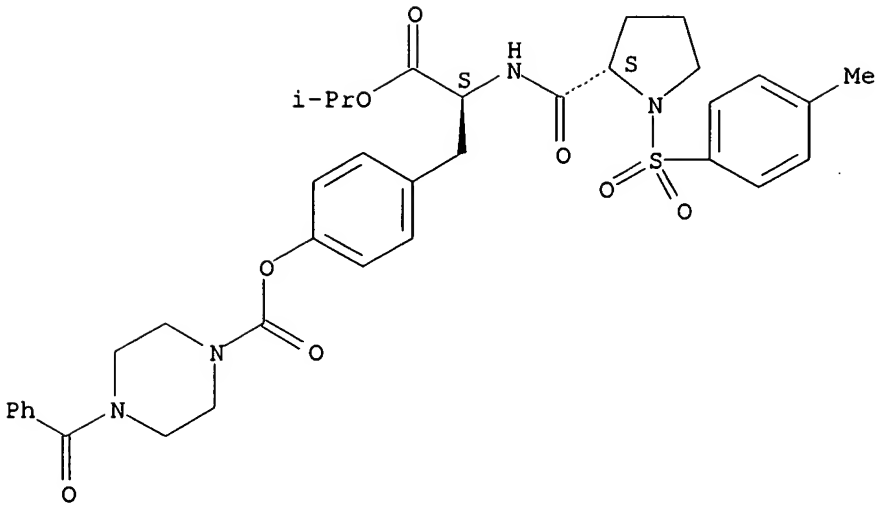
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

REFERENCE 2: 130:182768

L23 ANSWER 131 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220546-96-3** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1-methylethyl ester, 4-benzoyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H42 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

REFERENCE 2: 142:114469

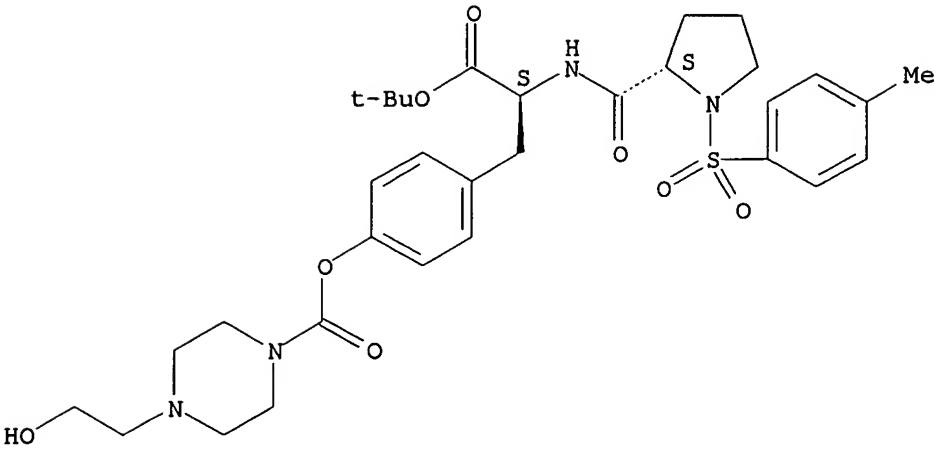
REFERENCE 3: 141:191071

REFERENCE 4: 141:191070

REFERENCE 5: 130:182768

L23 ANSWER 142 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220545-43-7** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 1,1-dimethylethyl ester, 4-(2-hydroxyethyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H44 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 142:114470

REFERENCE 2: 142:114469

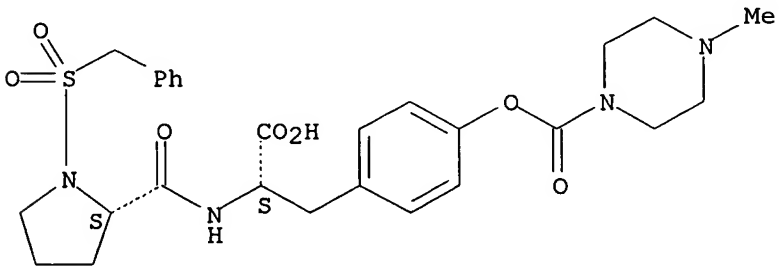
REFERENCE 3: 141:191071

REFERENCE 4: 141:191070

REFERENCE 5: 130:182768

L23 ANSWER 157 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220544-87-6** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, 1-[(phenylmethyl)sulfonyl]-L-prolyl-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H34 N4 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



Searcher : Shears 571-272-2528

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

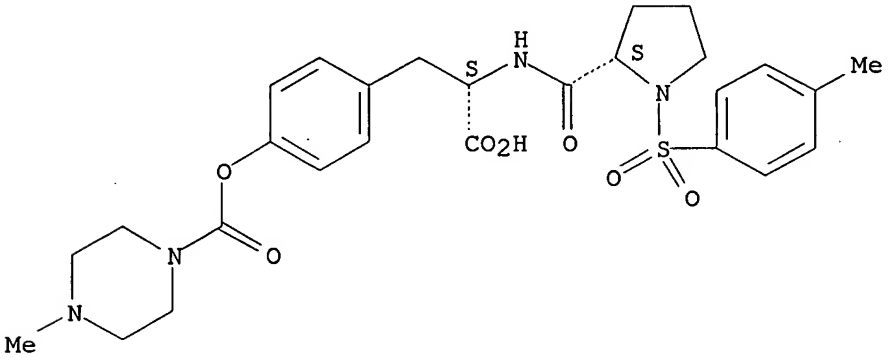
REFERENCE 1: 142:114470

REFERENCE 2: 141:191070

REFERENCE 3: 130:182768

L23 ANSWER 166 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN
RN **220543-95-3** REGISTRY
ED Entered STN: 18 Mar 1999
CN L-Tyrosine, 1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H34 N4 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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REFERENCE 2: 142:114469

REFERENCE 3: 142:48474

REFERENCE 4: 141:191071

REFERENCE 5: 141:191070

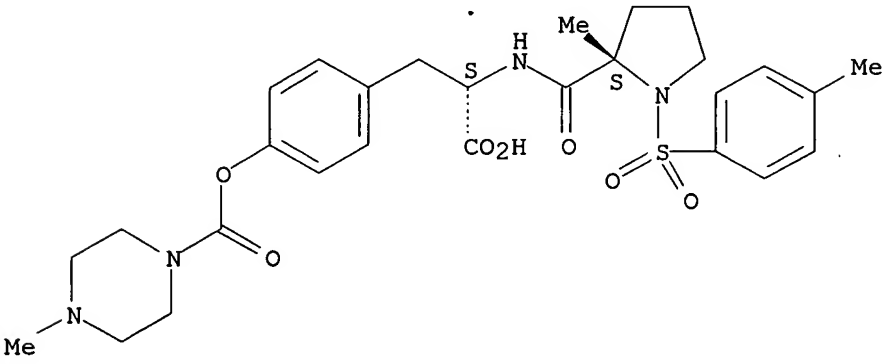
REFERENCE 6: 130:182768

REFERENCE 7: 130:177528

L23 ANSWER 170 OF 171 REGISTRY COPYRIGHT 2005 ACS on STN

RN **220173-41-1** REGISTRY
ED Entered STN: 04 Mar 1999
CN L-Tyrosine, 2-methyl-1-[(4-methylphenyl)sulfonyl]-L-prolyl-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H36 N4 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:153984

FILE 'CAOLD' ENTERED AT 11:01:47 ON 26 APR 2005
L24 0 S L23

FILE 'USPATFULL' ENTERED AT 11:01:55 ON 26 APR 2005
L25 14 S L23

L25 ANSWER 1 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2005:86989 USPATFULL
TITLE: Methods and compositions for treating rheumatoid arthritis
INVENTOR(S): Yednock, Theodore A., Forest Knolls, CA, UNITED STATES
Freedman, Stephen B., San Francisco, CA, UNITED STATES
Lieberburg, Ivan, Berkeley, CA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Konradi, Andrei W., San Francisco, CA, UNITED STATES
Shopp, George, South San Francisco, CA, UNITED STATES
Messersmith, Elizabeth, El Cerrito, CA, UNITED STATES
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., South San Francisco, CA, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005074451	A1	20050407	
APPLICATION INFO.:	US 2004-875469	A1	20040625	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-482211P	20030625	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 21901
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This application relates to methods and compositions for treating rheumatoid arthritis by administering a combination therapy comprising methotrexate and an antibody to alpha-4 integrin or an immunologically active antigen binding fragment in therapeutically effective amounts. The application also relates generally to methods and compositions for treating rheumatoid arthritis by administering a combination therapy comprising methotrexate and small molecule alpha-4 integrin antagonist that inhibits the alpha-4 integrin ($\alpha 4$ integrin) interaction with VCAM-1. The invention further relates to methods of preparing the compounds and methods of using the compounds and compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 2 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2005:81100 USPATFULL
TITLE: Composition for and treatment of demyelinating diseases and paralysis by administration of remyelinating agents
INVENTOR(S): Karlik, Stephen J., Ontario, CANADA
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Konradi, Andrei W., Burlingame, CA, UNITED STATES
Farouz, Francine S., Mercer Island, WA, UNITED STATES
Semko, Christopher M., Fremont, CA, UNITED STATES
Dressen, Darren B., San Mateo, CA, UNITED STATES
Messersmith, Elizabeth, El Cerrito, CA, UNITED STATES
Freedman, Stephen, San Francisco, CA, UNITED STATES
Yednock, Ted, Forest Knolls, CA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005069541	A1	20050331	
APPLICATION INFO.:	US 2004-763424	A1	20040126	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-442171P	20030124	(60)
	US 2003-500316P	20030905	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 59
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 25 Drawing Page(s)
LINE COUNT: 17044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The application provides for methods and compositions for inhibiting demyelination, promoting remyelination and/or treating paralysis in a subject in need thereof. Preferably, such compositions include immunoglobulins (e.g., antibodies, antibody fragments, and recombinantly produced antibodies or fragments), polypeptides (e.g., soluble forms of the ligand proteins for integrins) and small molecules, which when administered in an effective amount inhibits demyelination and/or promotes remyelination in a patient. The compositions and methods described herein can also utilize other anti-inflammatory agents used to palliate conditions and diseases associated with demyelination.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 3 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2005:75891 USPATFULL
TITLE: Methods and compositions for treating rheumatoid arthritis
INVENTOR(S): Yednock, Theodore A., Forest Knolls, CA, UNITED STATES
Freedman, Stephen B., San Francisco, CA, UNITED STATES
Lieberburg, Ivan, Berkeley, CA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Konradi, Andrei W., San Francisco, CA, UNITED STATES
Shopp, George, South San Francisco, CA, UNITED STATES
Messersmith, Elizabeth, El Cerrito, CA, UNITED STATES
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., South San Francisco, CA (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005065192	A1	20050324	
APPLICATION INFO.:	US 2004-875282	A1	20040625	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-482211P	20030625	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS DOANE SWECKER & MATHIS L L P, POST OFFICE BOX 1404, ALEXANDRIA, VA, 22313-1404
NUMBER OF CLAIMS: 123
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 24079
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This application relates to methods and compositions for treating rheumatoid arthritis by administering a combination therapy

comprising methotrexate and an antibody to alpha-4 integrin or an immunologically active antigen binding fragment in therapeutically effective amounts. The application also relates generally to methods and compositions for treating rheumatoid arthritis by administering a combination therapy comprising methotrexate and small molecule alpha-4 integrin antagonist that inhibits the alpha-4 integrin (α4 integrin) interaction with VCAM-1. The invention further relates to methods of preparing the compounds and methods of using the compounds and compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 4 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2004:204184 USPATFULL
TITLE: Tyrosine derivatives
INVENTOR(S): Jackson, David Y., San Bruno, CA, UNITED STATES
Sailes, Frederick C., Stone Mountain, GA, UNITED STATES
Sutherlin, Daniel P., San Carlos, CA, UNITED STATES
PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004158076	A1	20040812
APPLICATION INFO.:	US 2004-772678	A1	20040204 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2002-198328, filed on 16 Jul 2002, PENDING Continuation of Ser. No. US 2000-669779, filed on 25 Sep 2000, GRANTED, Pat. No. US 6469047

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-156062P	19990924 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA, 94080
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 2284
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The compounds of the invention are inhibitors of alpha4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 5 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2004:145080 USPATFULL
TITLE: Tyrosine derivatives
INVENTOR(S): Jackson, David Y., San Bruno, CA, UNITED STATES
Sailes, Frederick C., Stone Mountain, GA, UNITED STATES
Sutherlin, Daniel P., San Carlos, CA, UNITED STATES
PATENT ASSIGNEE(S): Genentech, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004110753	A1	20040610
APPLICATION INFO.:	US 2002-198328	A1	20020716 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-669779, filed on 25 Sep 2000, GRANTED, Pat. No. US 6469047

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-156062P	19990924 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA, 94080
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 1903
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The compounds of the invention are inhibitors of alpha4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 6 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2004:19373 USPATFULL
TITLE: Carbamyloxy compounds which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D., Moss Beach, CA, UNITED STATES
Semko, Christopher M., Fremont, CA, UNITED STATES
Sarantakis, Dimitrios, Newtown, PA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Kreft, Anthony, Langhorne, PA, UNITED STATES
Konradi, Andrei W., San Francisco, CA, UNITED STATES
Grant, Francine S., San Francisco, CA, UNITED STATES
Dressen, Darren B., San Mateo, CA, UNITED STATES
Ashwell, Susan, Plainsboro, NJ, UNITED STATES
Baudy, Reinhardt Bernhard, Doylestown, PA, UNITED STATES
Lombardo, Louis John, Belle Mead, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004014677	A1	20040122
APPLICATION INFO.:	US 2002-316205	A1	20021211 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-987900, filed on 16 Nov 2001, GRANTED, Pat. No. US 6525026 Division of Ser. No. US 1998-126958, filed on 31 Jul 1998, GRANTED, Pat. No. US 6489300

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-112020P	19970731 (60)
	US 1997-54453P	19970801 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gerald F. Swiss, Esq., BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 10469

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds which bind VLA4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 7 OF 14 USPATFULL on STN

ACCESSION NUMBER: 2003:38124 USPATFULL

TITLE: Pyroglutamic acid derivatives and related compounds which inhibit leukocyte adhesion mediated by VLA-4

INVENTOR(S): Dressen, Darren B., San Mateo, CA, UNITED STATES
Kreft, Anthony, Langhorne, PA, UNITED STATES
Kubrak, Dennis, Philadelphia, PA, UNITED STATES
Mann, Charles William, Philadelphia, PA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Stack, Gary Paul, Ambler, PA, UNITED STATES
Thorsett, Eugene D., Moss Beach, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003027771	A1	20030206
APPLICATION INFO.:	US 2002-139382	A1	20020507 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-489164, filed on 21 Jan 2000, GRANTED, Pat. No. US 6407066

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Gerald F. Swiss, BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

LINE COUNT: 5157

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are pyroglutamic acid derivatives and related compounds which bind VLA-4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 8 OF 14 USPATFULL on STN

ACCESSION NUMBER: 2003:24150 USPATFULL

TITLE: Carbamyloxy compounds which inhibit leukocyte adhesion mediated by VLA-4

INVENTOR(S): Thorsett, Eugene D., Moss Beach, CA, UNITED STATES
Semko, Christopher M., Fremont, CA, UNITED STATES

Sarantakis, Dimitrios, Newtown, PA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Kreft, Anthony, Langhorne, PA, UNITED STATES
Konradi, Andrei W., San Francisco, CA, UNITED STATES
Grant, Francine S., San Francisco, CA, UNITED STATES
Dressen, Darren B., San Mateo, CA, UNITED STATES
Ashwell, Susan, Plainsboro, NJ, UNITED STATES
Baudy, Reinhardt Bernhard, Doylestown, PA, UNITED STATES
Lombardo, Louis John, Belle Mead, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003017993	A1	20030123
	US 6525026	B2	20030225
APPLICATION INFO.:	US 2001-987900	A1	20011116 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-126958, filed on 31 Jul 1998, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-54453P	19970801 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 10392
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds which bind VLA-4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 9 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:337947 USPATFULL
TITLE: Carbamyloxy compounds which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D., Moss Beach, CA, UNITED STATES
Semko, Christopher M., Fremont, CA, UNITED STATES
Sarantakis, Dimitrios, Newtown, PA, UNITED STATES
Pleiss, Michael A., Sunnyvale, CA, UNITED STATES
Kreft, Anthony, Langhorne, PA, UNITED STATES
Konradi, Andrei W., San Francisco, CA, UNITED STATES
Grant, Francine S., San Francisco, CA, UNITED STATES
Dressen, Darren B., San Mateo, CA, UNITED STATES
Ashwell, Susan, Plainsboro, NJ, UNITED STATES

Baudy, Reinhardt Bernhard, Doylestown, PA, UNITED STATES
Lombardo, Louis John, Belle Mead, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002193312	A1	20021219
APPLICATION INFO.:	US 2001-987619	A1	20011115 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1998-126958, filed on 31 Jul 1998, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-54453P	19970801 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gerald F. Swiss, BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box 1404, Alexandria, VA, 22313-1404
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 10499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds which bind VLA-4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 10 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:317409 USPATFULL
TITLE: Carbamyloxy compounds which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Thorsett, Eugene D., 571 Buena Vista, Moss Beach, CA, United States 94038
Semko, Christopher M., 2361 Carpenter Ct., Fremont, CA, United States 94539
Sarantakis, Dimitrios, 262 Sentinel Ave., Newtown, PA, United States 18940
Pleiss, Michael A., 848 Stella Ct., Sunnyvale, CA, United States 94087
Kreft, Anthony, 43 Barley Ct., Langhorne, PA, United States 19047
Konradi, Andrei W., 95 Cervantes #105, San Francisco, CA, United States 94123
Grant, Francine S., 3735 Sacramento St., San Francisco, CA, United States 94118
Dressen, Darren B., 3110 Casa De Campo #2, San Mateo, CA, United States 94403
Ashwell, Susan, 1015 Aspen Dr., Plainsboro, NJ, United States 08536
Baudy, Reinhardt Bernhard, 5281 Harrington Ct., Doylestown, PA, United States 18901
Lombardo, Louis John, 412 S. Woods Rd., Belle Mead,

NJ, United States 08502

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6489300	B1	20021203
APPLICATION INFO.:	US 1998-126958		19980731 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-54453P	19970801 (60)
	US 1997-112020P	19970731 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Low, Christopher S. F.
ASSISTANT EXAMINER: Lukton, David
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis LLP
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 9372
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are compounds which bind VLA-4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 11 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:276118 USPATFULL
TITLE: Tyrosine derivatives
INVENTOR(S): Jackson, David Y., San Bruno, CA, United States
Sailes, Frederick C., Stone Mountain, GA, United States
Sutherlin, Daniel P., San Carlos, CA, United States
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6469047	B1	20021022
APPLICATION INFO.:	US 2000-669779		20000925 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-156062P	19990924 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Seaman, D. Margaret
LEGAL REPRESENTATIVE: Evans, David W
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 1413

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The compounds of the invention are inhibitors of alpha4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 12 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:144241 USPATFULL
TITLE: Pyroglutamic acid derivatives and related compounds which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Dressen, Darren B., San Mateo, CA, United States
Kreft, Anthony, Langhorne, PA, United States
Kubrak, Dennis, Philadelphia, PA, United States
Mann, Charles William, Philadelphia, PA, United States
Pleiss, Michael A., Sunnyvale, CA, United States
Stack, Gary Paul, Ambler, PA, United States
Thorsett, Eugene D., Moss Beach, CA, United States
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., South San Francisco, CA, United States (U.S. corporation)
American Home Products Corporation, Madison, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6407066	B1	20020618	
APPLICATION INFO.:	US 2000-489164		20000121	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-198244P	19990126 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Lukton, David
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis LLP
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT: 4702
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are pyroglutamic acid derivatives and related compounds which bind VLA-4. Certain of these compounds also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compounds are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compounds can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 13 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2002:72608 USPATFULL
TITLE: ANTI-INFLAMMATORY COMPOSITIONS AND METHOD
INVENTOR(S): YEDNOCK, THEODORE A., FOREST KNOLLS, CA, UNITED STATES
PLEISS, MICHAEL A., SUNNYVALE, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002039745	A1	20020404
APPLICATION INFO.:	US 1998-127364	A1	19980731 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1997-904424, filed on 31 Jul 1997, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-54453P	19970801 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GERALD F. SWISS ESQ., BURNS, DOANE, SWECKER & MATHIS LLP, P.O. BOX 1404, ALEXANDRIA, VA, 22313
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Page(s)
LINE COUNT: 2015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The disclosed invention includes pharmaceutical compositions and methods for treating inflammatory conditions, particularly those that are characterized by increased binding of alpha-9 integrin to one or more of its ligands. Also disclosed are methods for selecting compounds for use in such compositions and methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 14 OF 14 USPATFULL on STN
ACCESSION NUMBER: 2000:174676 USPATFULL
TITLE: 3,4-diamino-3-cyclobutene-1,2-dione derivatives which inhibit leukocyte adhesion mediated by VLA-4
INVENTOR(S): Lombardo, Louis J., Belle Mead, NJ, United States
Sabalski, Joan, Hamilton, NJ, United States
PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6166050		20001226
APPLICATION INFO.:	US 1999-458852		19991210 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-155221P	19981214 (60)

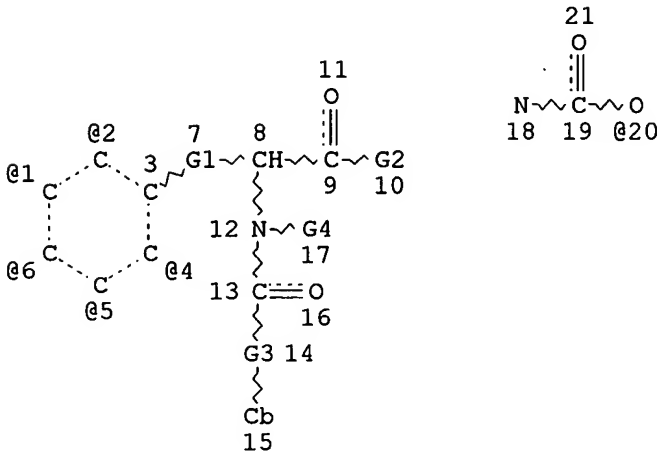
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Davis, Zinna Northington
LEGAL REPRESENTATIVE: Barrett, Rebbeca R.
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
LINE COUNT: 1459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of the formula ##STR1## which inhibit leukocyte adhesion mediated by interaction of the α.sub.4 β.sub.1 integrin (VLA-4) with its counterreceptor VCAM-1, and their use for the treatment of inflammatory and autoimmune diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 11:02:58 ON 26 APR 2005)
L26 0 S L23

(FILE 'REGISTRY' ENTERED AT 11:03:36 ON 26 APR 2005)
L15 STR



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REP G3=(0-4) C
VAR G4=H/AK
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NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE
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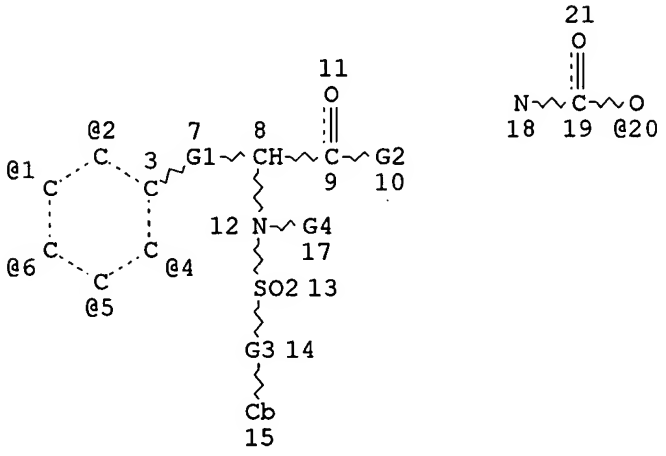

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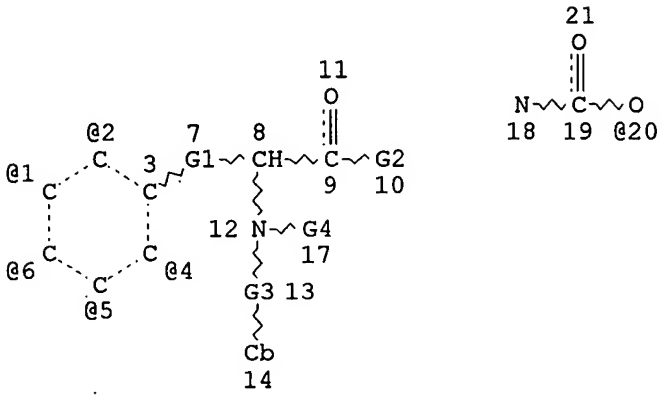
REP G3=(0-4) C
VAR G4=H/AK
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L17 STR



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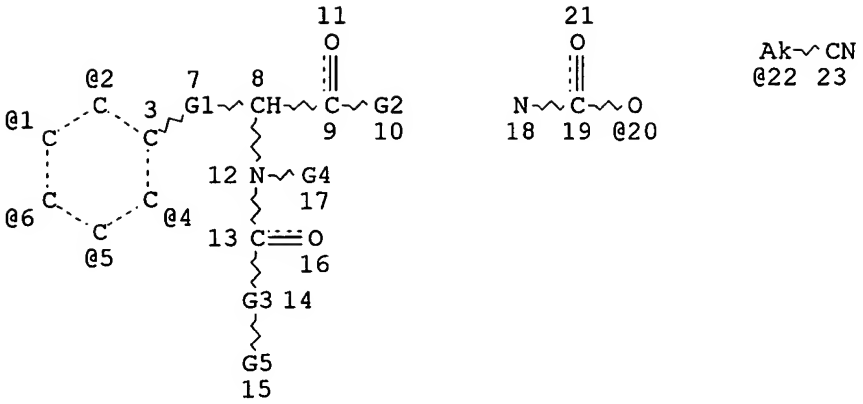
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 14
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

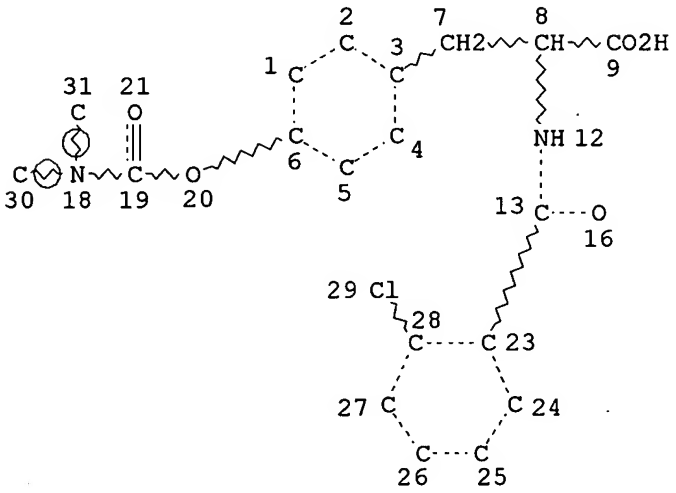
STEREO ATTRIBUTES: NONE
L18 STR



REP G1=(1-2) CH2
VAR G2=H/O/N/AK/HY
REP G3=(0-4) C
VAR G4=H/AK
VAR G5=22/CY
VPA 20-1/2/4/5/6 U
NODE ATTRIBUTES:
NSPEC IS R AT 18
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE
L19 541 SEA FILE=REGISTRY SSS FUL L15 OR L16 OR L17 OR L18
L27 STR



NODE ATTRIBUTES:
CONNECT IS X2 RC AT 1
CONNECT IS X2 RC AT 2
CONNECT IS X2 RC AT 4
CONNECT IS X2 RC AT 5

Searcher : Shears 571-272-2528

CONNECT IS X2 RC AT 24
CONNECT IS X2 RC AT 25
CONNECT IS X2 RC AT 26
CONNECT IS X2 RC AT 27
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 25

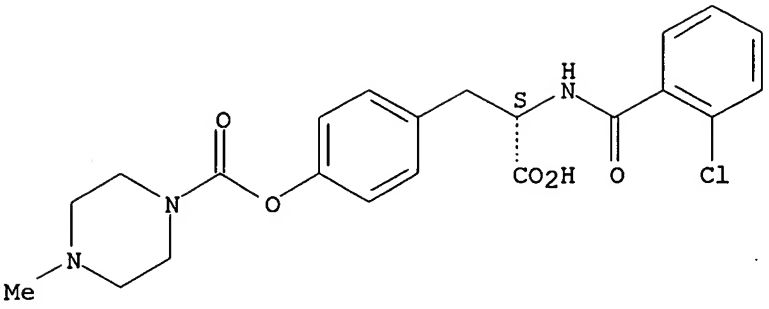
STEREO ATTRIBUTES: NONE
L28 31 SEA FILE=REGISTRY SUB=L19 SSS FUL L27

100.0% PROCESSED 169 ITERATIONS 31 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 11:10:12 ON 26 APR 2005
L29 2 S L28

L29 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:732382 CAPLUS
DOCUMENT NUMBER: 138:313904
TITLE: Solid-phase synthesis of dual α4β1/α4β7 integrin antagonists: two scaffolds with overlapping pharmacophores
AUTHOR(S): Castanedo, Georgette M.; Sailes, Fredrick C.; Dubree, Nathan J. P.; Nicholas, John B.; Caris, Lisa; Clark, Kevin; Keating, Susan M.; Beresini, Maureen H.; Chiu, Henry; Fong, Sherman; Marsters, James C.; Jackson, David Y.; Sutherlin, Daniel P.
CORPORATE SOURCE: Department of Bioorganic Chemistry, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2913-2917
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:313904
AB Two structural classes of dual α4β1/α4β7 integrin antagonists were investigated via solid-phase parallel synthesis. Using an acylated amino acid backbone, lead compds. containing biphenylalanine or tyrosine carbamate scaffolds were optimized for inhibition of α4β1/VCAM and α4β7/MAdCAM. A comparison of the structure-activity relationships in the inhibition of the α4β7/MAdCAM interaction for substituted amines employed in both scaffolds suggests a similar binding mode for the compds.
IT **331469-49-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of dual α4β1/α4β7 integrin antagonists)
RN 331469-49-9 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:228855 CAPLUS
DOCUMENT NUMBER: 134:252658
TITLE: Preparation of tyrosine derivatives as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.
INVENTOR(S): Jackson, David Y.; Sailes, Frederick C.; Sutherlin, Daniel P.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021584	A1	20010329	WO 2000-US26326	20000925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2385882	AA	20010329	CA 2000-2385882	20000925
EP 1214292	A1	20020619	EP 2000-965417	20000925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6469047	B1	20021022	US 2000-669779	20000925
JP 2003509488	T2	20030311	JP 2001-524964	20000925
US 2004110753	A1	20040610	US 2002-198328	20020716
US 2004158076	A1	20040812	US 2004-772678	20040204
PRIORITY APPLN. INFO.:			US 1999-156062P	P 19990924

US 2000-669779 A1 20000925

WO 2000-US26326 W 20000925

US 2002-198328 A1 20020716

OTHER SOURCE(S): MARPAT 134:252658

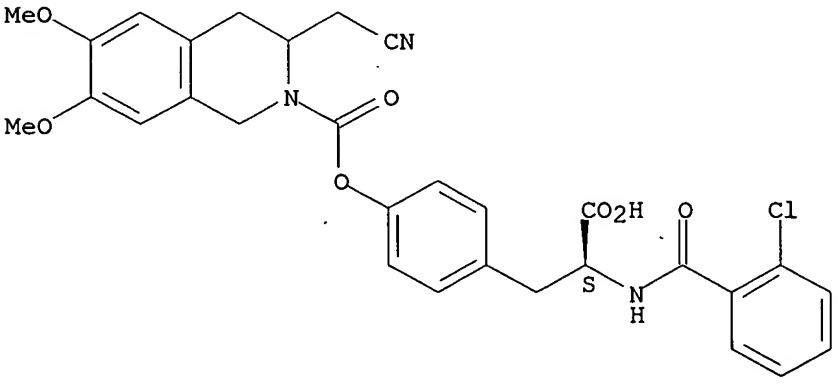
AB Tyrosine derivs., e.g., ArCH2CH[N(A)(Z)]CO-Y [Z = H, alkyl; A = B(CH2)q-X-, where B = (un)substituted Ph and X = CO, SO2, null or B = cyanoalkyl, carbocyclyl or heterocyclyl and X = CO; R6 = H, alkyl, amino, cyano, hydroxy, alkylsulfonyl, etc.; q = 0-3; Y is H, (un)substituted alkoxy, alkoxyalkoxy, aryloxy, alkylaminoalkoxy, dialkylaminoalkoxy,alkylamino, arylamino, heterocyclyl or heteroarylalkyl; Ar is Ph which has hydroxy, carbonate, thiocarbonate, carbamoyloxy or acyloxy groups and optionally other substituents] were prepared as inhibitors of α4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM. Methods of synthesis are described and inhibitory binding data are tabulated for 416 compds., including N-(o-chlorobenzoyl)-O-(allylcarbamoyl)-L-tyrosine, for which IC50 is < 1.0 micromolar.

IT **331468-18-9P 331468-24-7P 331468-25-8P**
331468-26-9P 331468-27-0P 331468-28-1P
331468-29-2P 331468-30-5P 331468-31-6P
331468-32-7P 331468-34-9P 331468-35-0P
331468-38-3P 331468-39-4P 331468-40-7P
331469-12-6P 331469-40-0P 331469-41-1P
331469-46-6P 331469-49-9P 331469-50-2P
331469-51-3P 331469-52-4P 331469-75-1P
331469-76-2P 331469-77-3P 331469-78-4P
331469-79-5P 331469-80-8P 331469-81-9P
331469-90-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.)

RN 331468-18-9 CAPLUS

CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3-(cyanomethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

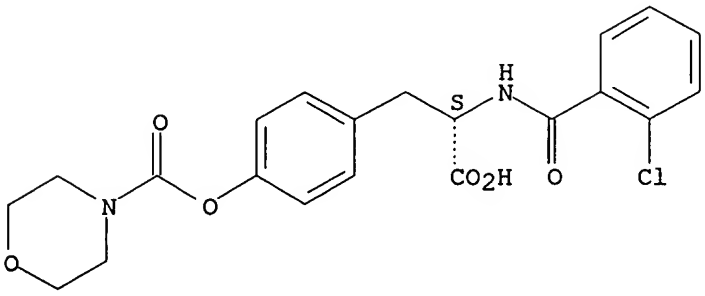
Absolute stereochemistry.



RN 331468-24-7 CAPLUS

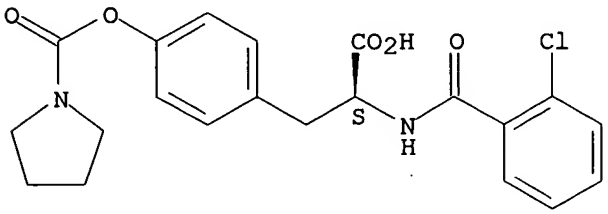
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-morpholinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



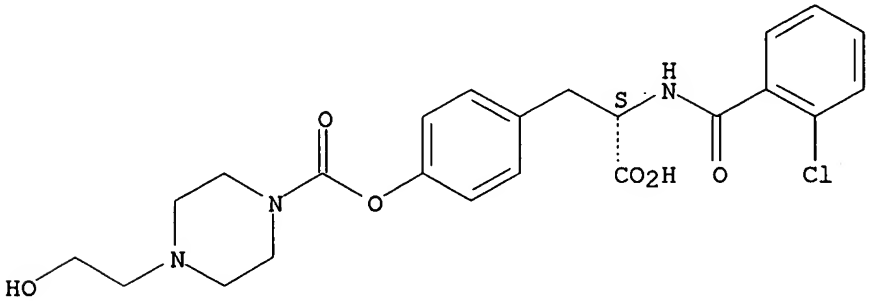
RN 331468-25-8 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 1-pyrrolidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



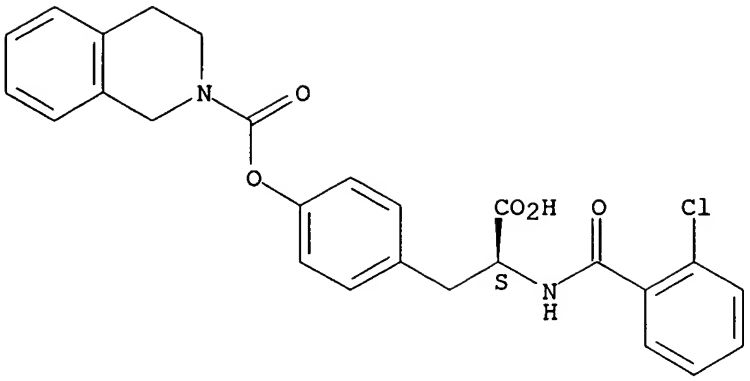
RN 331468-26-9 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-(2-hydroxyethyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



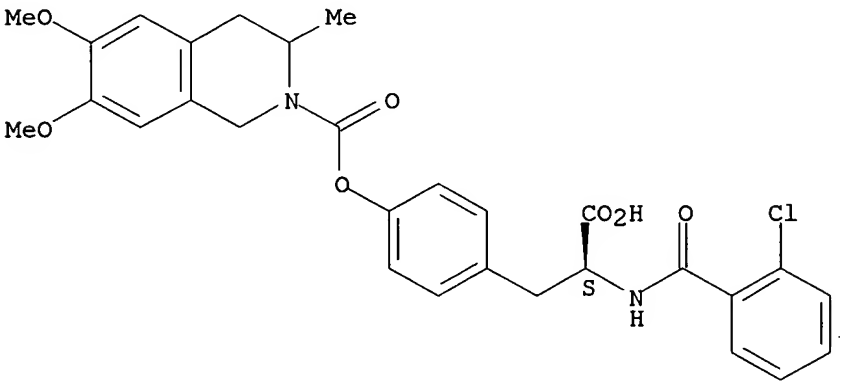
RN 331468-27-0 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



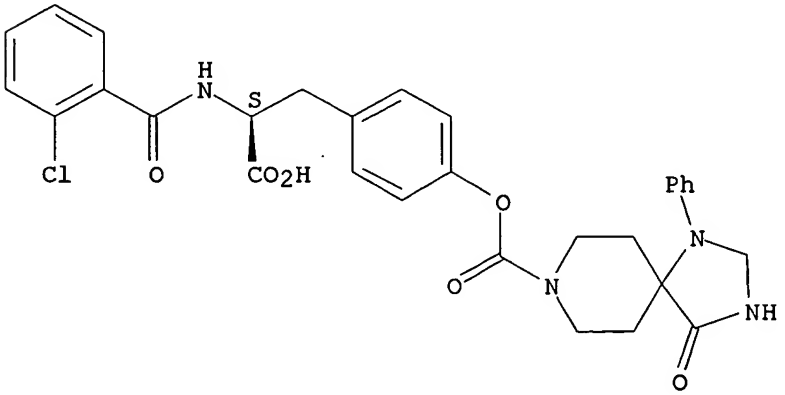
RN 331468-28-1 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-3-methyl-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331468-29-2 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decane-8-carboxylate (ester) (9CI) (CA INDEX NAME)

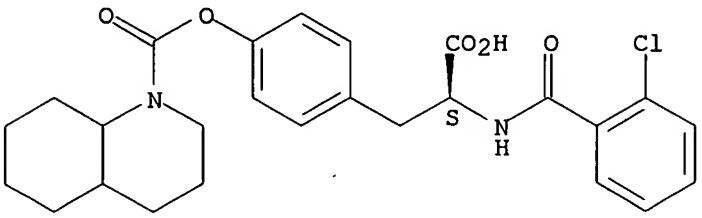
Absolute stereochemistry.



Searcher : Shears 571-272-2528

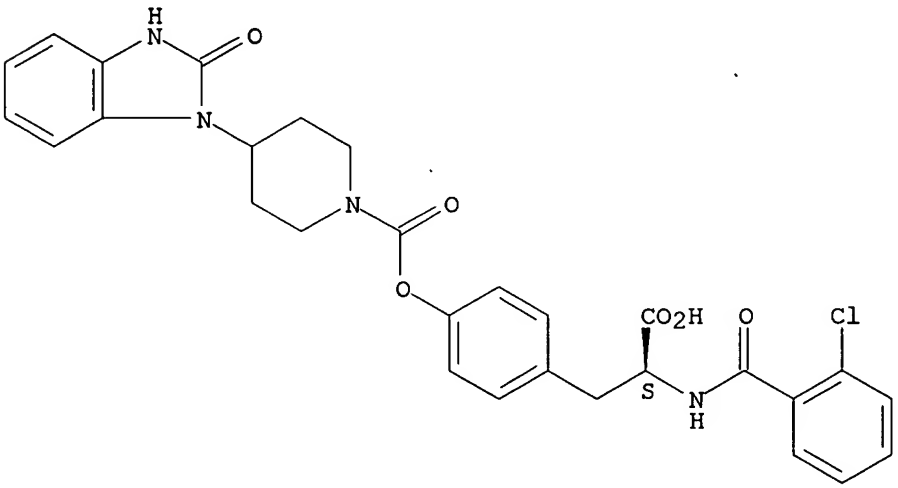
RN 331468-30-5 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, octahydro-1(2H)-quinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



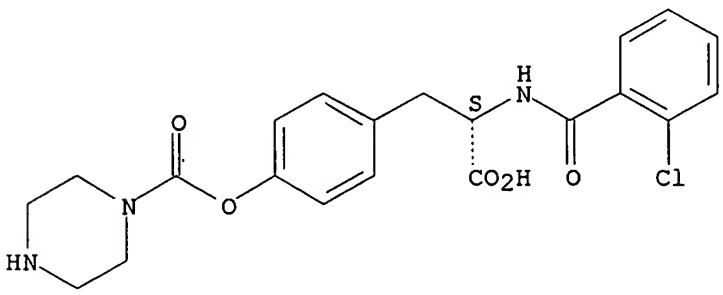
RN 331468-31-6 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl)-1-piperidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



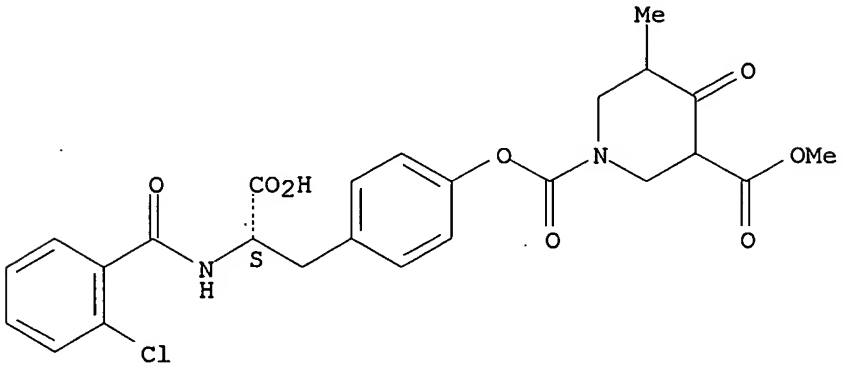
RN 331468-32-7 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



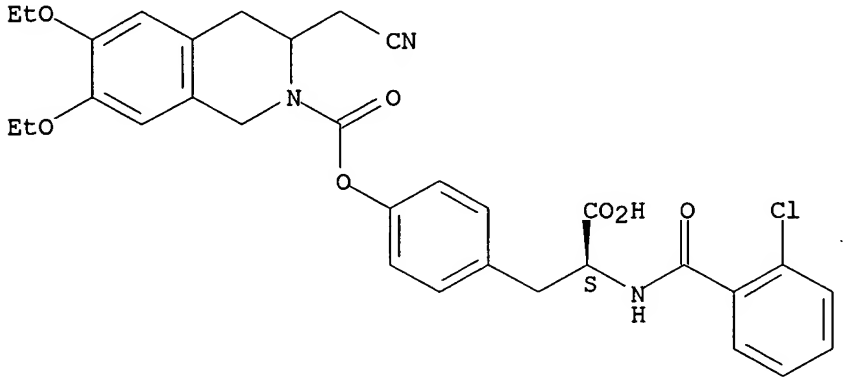
RN 331468-34-9 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3-methyl 5-methyl-4-oxo-1,3-piperidinedicarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



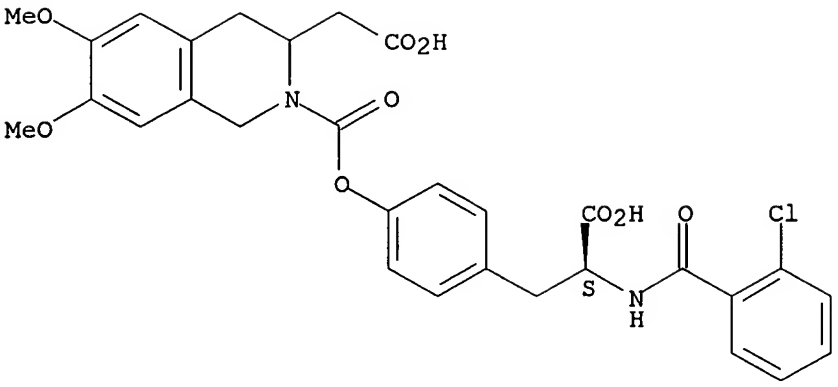
RN 331468-35-0 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3-(cyanomethyl)-6,7-diethoxy-3,4-dihydro-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



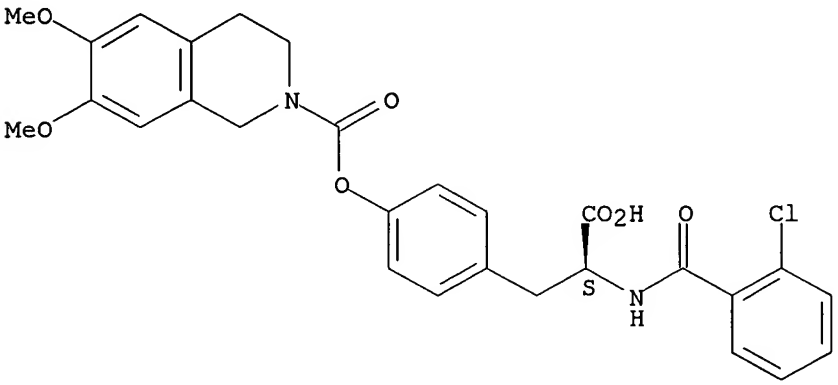
RN 331468-38-3 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3-(carboxymethyl)-3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



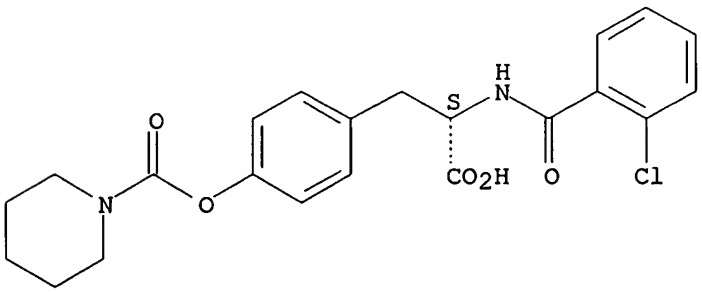
RN 331468-39-4 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331468-40-7 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 1-piperidinecarboxylate (ester) (9CI) (CA INDEX NAME)

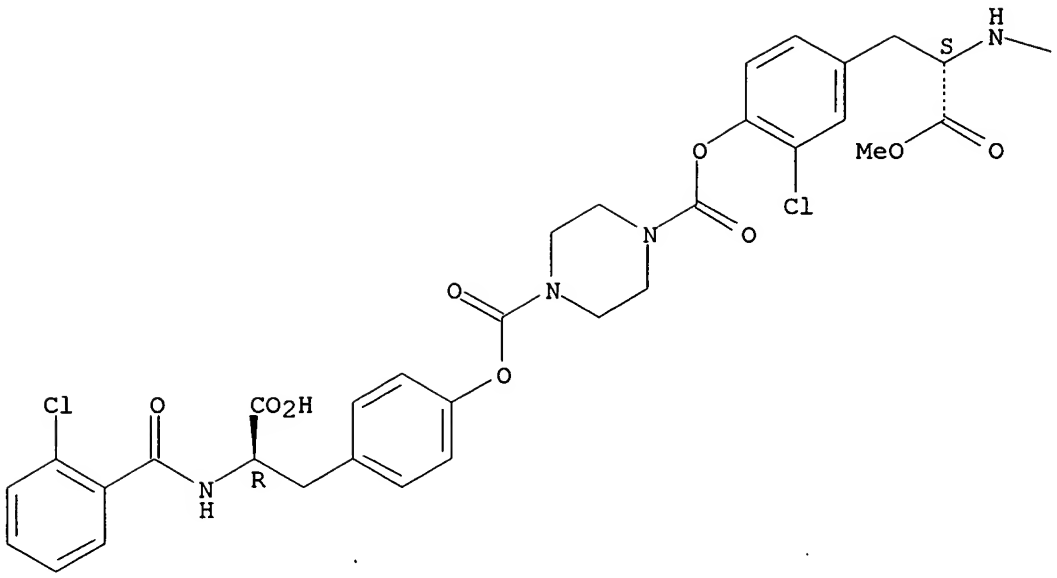
Absolute stereochemistry.



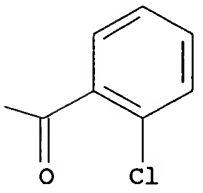
RN 331469-12-6 CAPLUS
CN D-Tyrosine, N-(2-chlorobenzoyl)-, ester with 3-chloro-N-(2-chlorobenzoyl)-L-tyrosine methyl ester hydrogen 1,4-piperazinedicarboxylate (ester) (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

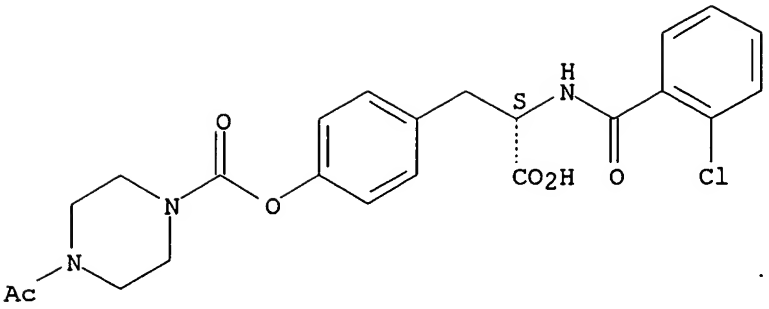


PAGE 1-B



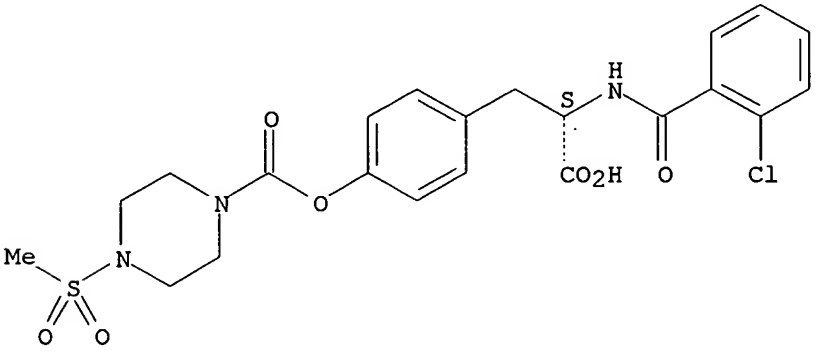
RN 331469-40-0 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-acetyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331469-41-1 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-(methylsulfonyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

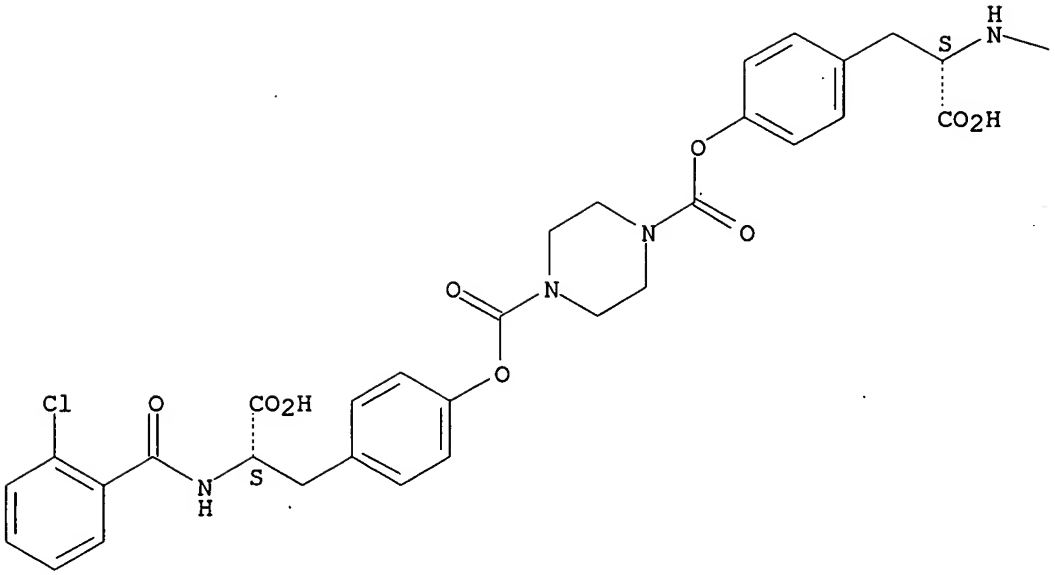
Absolute stereochemistry.



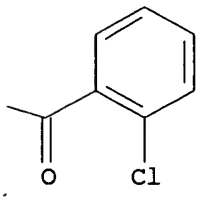
RN 331469-46-6 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 1,4-piperazinedicarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

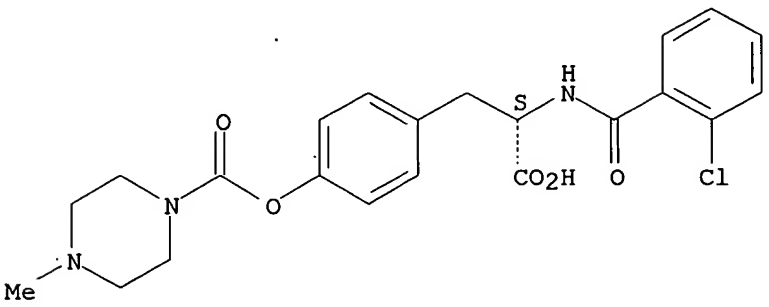


PAGE 1-B



RN 331469-49-9 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-methyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

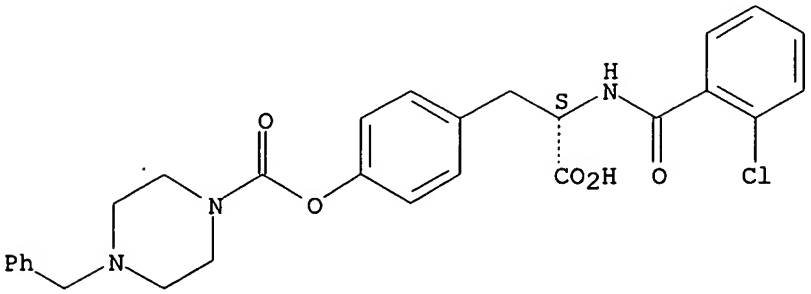
Absolute stereochemistry.



Searcher : Shears 571-272-2528

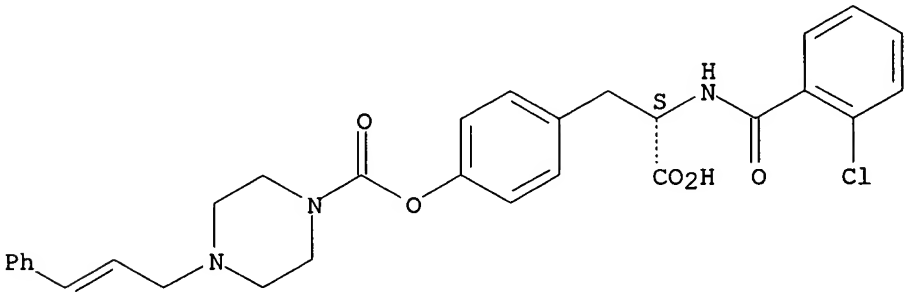
RN 331469-50-2 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-(phenylmethyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



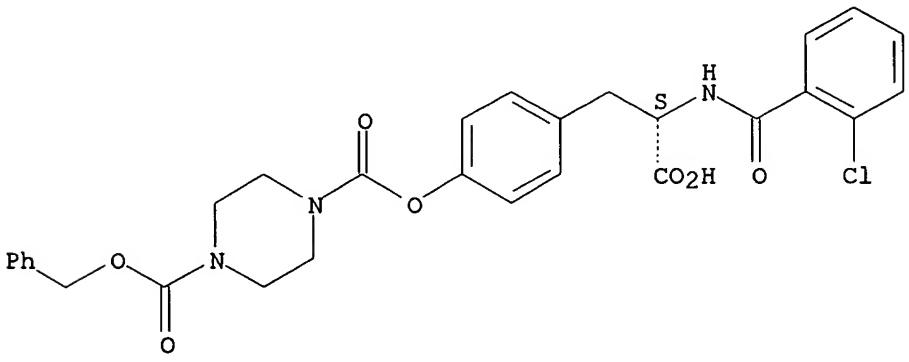
RN 331469-51-3 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-(3-phenyl-2-propenyl)-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 331469-52-4 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, phenylmethyl 1,4-piperazinedicarboxylate (ester) (9CI) (CA INDEX NAME)

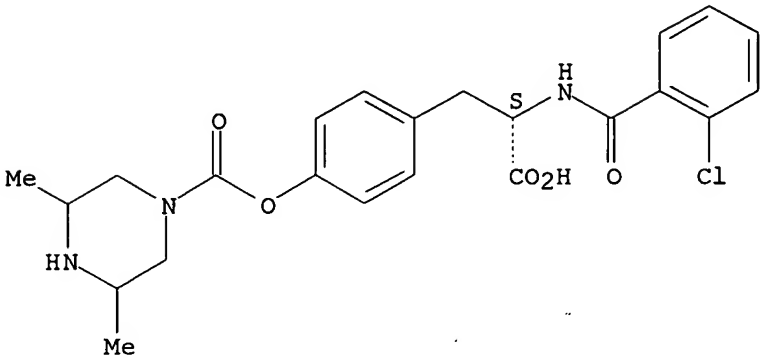
Absolute stereochemistry.



RN 331469-75-1 CAPLUS

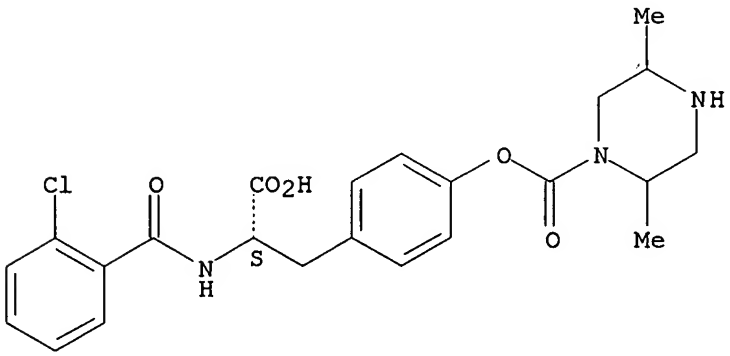
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,5-dimethyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



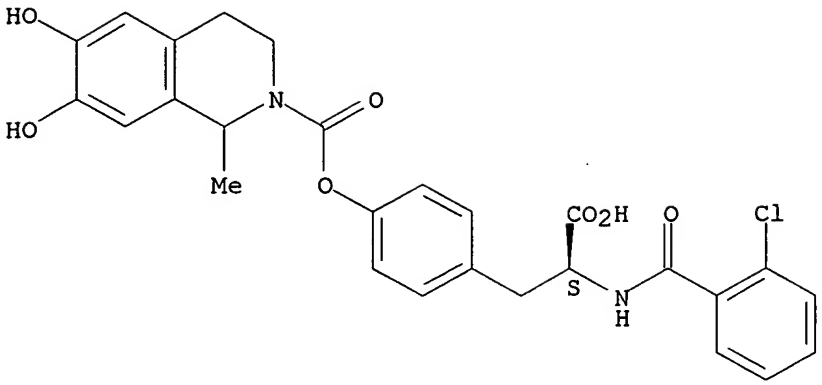
RN 331469-76-2 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 2,5-dimethyl-1-piperazinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



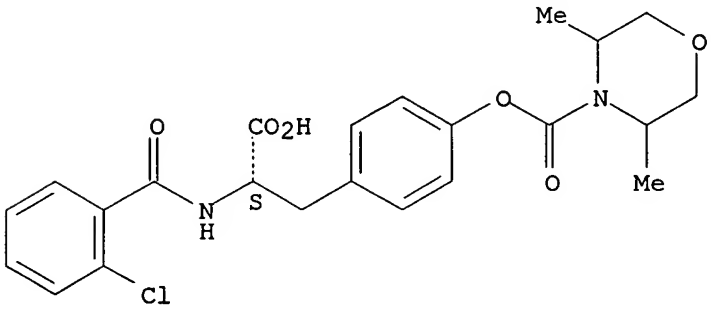
RN 331469-77-3 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dihydroxy-1-methyl-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



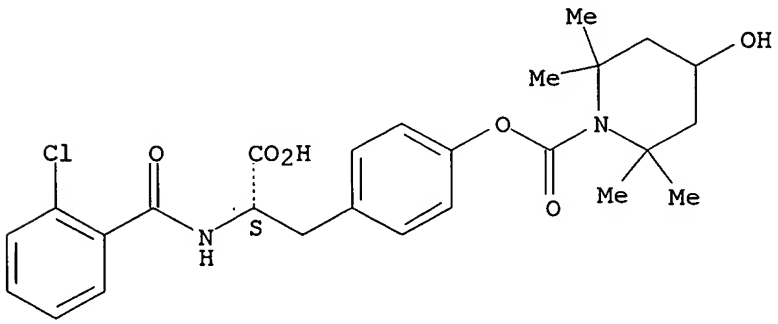
RN 331469-78-4 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,5-dimethyl-4-morpholinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



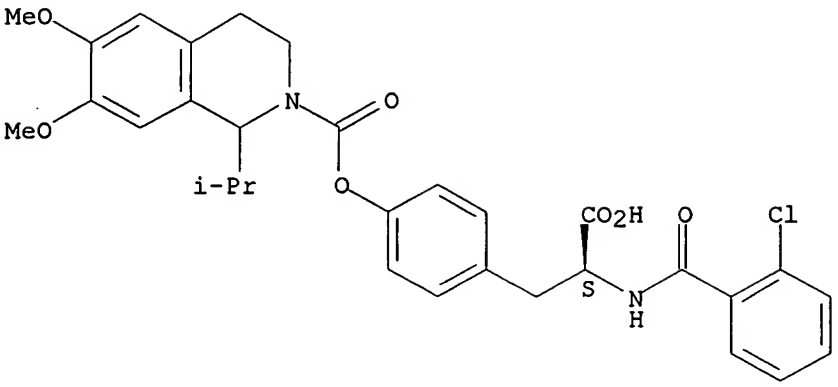
RN 331469-79-5 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 4-hydroxy-2,2,6,6-tetramethyl-1-piperidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



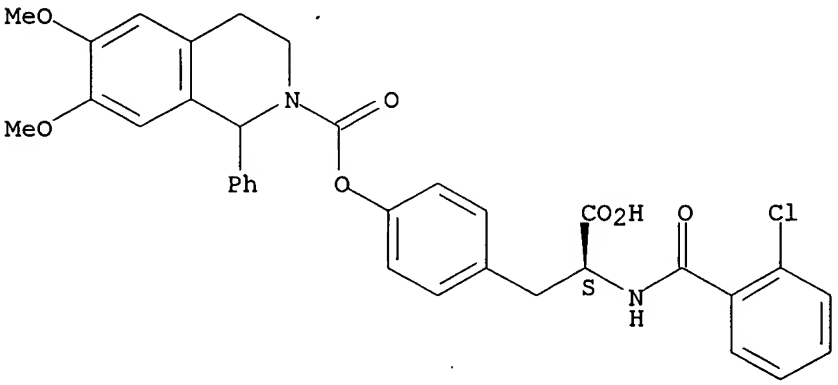
RN 331469-80-8 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-1-(1-methylethyl)-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



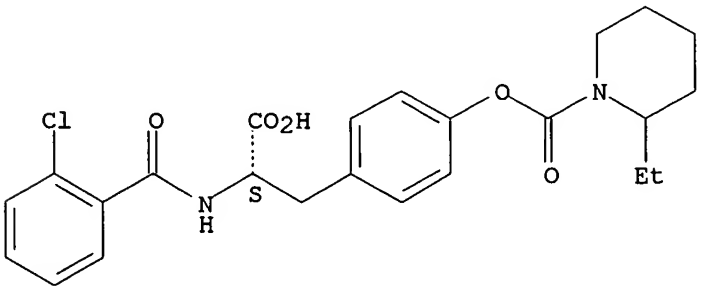
RN 331469-81-9 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 3,4-dihydro-6,7-dimethoxy-1-phenyl-2(1H)-isoquinolinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 331469-90-0 CAPLUS
CN L-Tyrosine, N-(2-chlorobenzoyl)-, 2-ethyl-1-piperidinecarboxylate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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